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# Magnetoencephalographic (MEG) Inter-subject Correlation using Continuous Music Stimuli

**School of Science**

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ABSTRACT OF THE
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Music has existed throughout cultures for thousands of years and has been able to create powerful and intercultural connections between humans. Yet, early neurocognitive studies on music have utilized mainly artificial stimuli. Going towards more complex, real-world stimuli, this study examines magnetoencephalographic (MEG) brain responses to listening to continuous music in 24 musically trained and 19 untrained listeners. Three whole musical pieces of different genres were presented as stimuli. To investigate how similarly listeners' brains process the music, inter-subject correlations (ISC) of the dynamics of specific MEG frequency bands were computed. This approach is a novel method for analyzing complex stimuli with MEG. Compared to functional magnetic resonance imaging (fMRI) studies, it adds to the information about synchronous processing of continuous music stimuli in the brain. Our MEG results show that auditory processing areas, including middle and superior temporal gyri, transverse temporal cortex and insula with enhanced right hemispheric responses, synchronize across subjects. The extend of synchronization differs depending on the selected frequency band and music stimulus. For the song that elicited highest ISCs across subjects, in the 4–8 Hz and 8–12 Hz frequency bands, musicians exhibit higher synchrony in auditory processing areas compared to non-musicians. In summary, listening to real music induces brain-to-brain coupling especially in auditory cortices. Coupling in musicians during listening to a piece with a variety and complexity of musical features is higher compared to non-trained participants.

Keywords: Music, Continuous Stimuli, MEG, Inter-subject Correlation, Musical Expertise, Naturalistic Stimuli

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Tuhansien vuosien ajan musiikki on ollut olemassa eri kulttuureissa ja kyennyt luomaan voimakkaita ja kulttuurienvälisiä yhteyksiä ihmisten välille. Varhaisessa neurokognitiivisessa musiikkitutkimuksessa käytettiin pääasiassa keinotekoisia ärsykkeitä. Tässä tutkimuksessa käytetään monimutkaisia tosielämän ärsykkeitä esittämällä 43 koehenkilölle kolme musiikkikappaletta ja mittaamalla samalla aivovasteita magnetoenkefalografialla (MEG). Osa koehenkilöistä oli musiikillisesti harjaantuneita ja osa harjaantumattomia. Jotta voitaisiin tutkia, kuinka samalla tavalla kuuntelijoiden aivot käsittelevät musiikkia, valikoiduista MEG-taajuuskaistoista laskettiin koehenkilöiden välinen korrelaatio (inter-subject correlation; ISC). Tämä lähestymistapa on uusi menetelmä monimutkaisten ärsykkeiden tutkimiseen MEG:llä. Funktionaaliseen magneettikuvaukseen (fMRI) verrattuna MEG vahvistaa ja täydentää tietoa jatkuvan musiikin synkronisesta prosessoimisesta aivoissa. Vasteet auditiivisilla prosessointialueilla, joihin sisältyvät keskimmäinen ja ylempi temporaalinen aivopoimu, poikittainen temporaalinen aivokuori ja aivosaari, synkronoituivat osallistujien välillä ja kasvoivat etenkin oikealla aivopuoliskolla. Synkronoitumisen laajuus vaihteli riippuen valitusta taajuuskaistasta ja musiikkiärsykkeestä. Suurimman ISC:n aiheuttanutta musiikkikappaletta kuunneltaessa muusikoiden auditiiviset prosessointialueet synkronoituivat matalalla taajuuskaistalla ei-muusikoiden vastaavia enemmän. ISC tarjoaa käyttökelpoisen metodin monimutkaisten tosielämän ärsykkeiden tutkimiseen MEG:llä ja saattaa näin ollen valottaa musiikin kulttuurisen ja yhteiskunnallisen tärkeyden neuraalista perustaa.

Avainsanat: musiikki, jatkuvat ärsykkeet, MEG, koehenkilöiden välinen korrelaatio, musiikillinen asiantuntemus, luonnollinen ärsyke

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Otaniemi, 21.10.2014

Anja Thiede

# Contents

# Symbols and abbreviations

## Operators

| | |
|---|---|
| $\text{argmin}_f(x)$ | gives the point $x_{min}$ at which f is minimized |
| $\|\|\mathbf{x}\|\|$ | norm of vector $\mathbf{x}$ |

## Abbreviations

| | |
|---|---|
| A1 | primary auditory cortex |
| BA6 | Brodmann area 6 |
| BOLD | blood oxygenation level dependent |
| ECoG | electrocorticography |
| EOG | electrooculogram |
| ERP | event-related potential |
| fMRI | functional magnetic resonance imaging |
| HG | Heschl's gyrus |
| HPI | head-position indicator |
| LFP | local field potential |
| MBEA | Montreal Battery of Evaluation of Amusia |
| M-CCA | multi-set canonical correlation analysis |
| MEG | magnetoencephalography |
| MNE | minimum norm estimation |
| MPRAGE | magnetization-prepared rapid acquisition of gradient echo |
| MRI | magnetic resonance imaging |
| SSS | signal space separation |
| SSP | signal space projection |
| STG | superior temporal gyrus |
| STS | superior temporal sulcus |
| SQUID | Superconducting Quantum Interference Device |

# 1 Introduction

## 1.1 Overview and Motivation

Music has existed throughout different cultures for thousands of years and has had an important impact. It has been able to create powerful and intercultural connections between humans and still does, possibly more than ever. Music is able to evoke strong emotions, which is often the reason why human beings listen to music in the first place. Nowadays, it is part of the everyday life of many people, and the complexity and variety of musical pieces and genres has grown exponentially. Neurocognitive studies have been addressing questions in different fields in music research. The trend is moving from the analysis of pure tones to identify the auditory processing path, to auditory feature analysis (e.g., melody, harmony, pitch, timbre), and nowadays goes towards using complex stimuli, such as whole musical pieces. Musical expertise is one of the prime examples of the ability of the brain to induce plastic changes (Pantev and Herholz, 2011) and even anatomical differences have been shown after long-term musical training (Schlaug et al., 1995a). In this study, following the trend of going away from artificial stimuli to real-world music, brain responses to whole pieces of music in 43 musically trained and untrained listeners are investigated by magnetoencephalography (MEG). The participants listened to three real musical pieces of different genres. To investigate how similarly listeners' brains process the music, inter-subject correlations (ISC) of the dynamics of specific MEG frequency bands were computed. The use of continuous stimuli and ISC in MEG is novel. Compared with functional magnetic resonance imaging (fMRI) studies, the higher temporal resolution of MEG could reveal synchronizations at finer temporal scales. Therefore, this study can complete the information about synchronous processing of continuous music stimuli in the brain. The results will likely provide insight to the processing of real-world stimuli, shed light on brain-to-brain coupling during music perception and improve the understanding about shared neural responses to music depending on musical expertise.

## 1.2 Background and Previous Work

### 1.2.1 Music and the Brain

In early stages of human society, music was used as a form of communication and it was a part of tribal rituals that symbolized the most important stages in life. Music can influence human development in a beneficial way in several, also non-music related aspects. It is used in therapeutic approaches, because of cross-modal, positive effects on several mind and body functions resulting from listening to or playing music. From a neuroscientific perspective, these are only a few reasons why it is interesting to study the underlying neural correlates of music. In the following, a short introduction about advances in cognitive music research shall be given. Thereafter, the influence of musical expertise on processing music in the brain will be discussed.

## Neural Correlates of Music Processing

Listening to music is connected to multiple senses and a variety of activations in different areas of the brain (Figure 1).

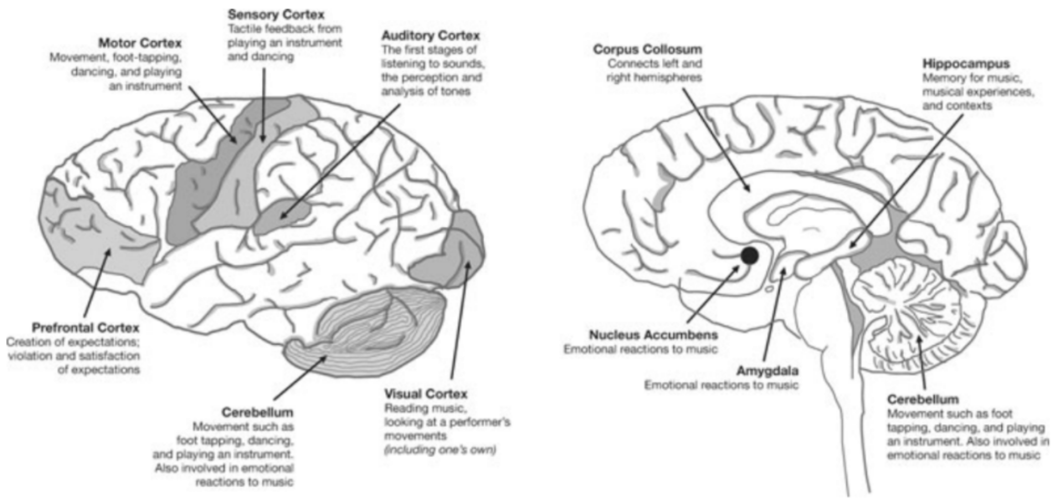



Figure 1: Brain areas engaged in processing of music. (Based on Tramo, 2001, updated from Levitin, 2006)

The perception of music begins with transducting the acoustic signal to a neural signal in the cochlea (inner ear). From there, the neural signal is transferred through the auditory nerve upstream to the superior olivary complex, which extracts differences in timing and intensity, and the inferior colliculus, where initial spectral processing takes place. From the medial geniculate body of the thalamus, the auditory information is mainly projected to the auditory cortices (Figure 2), but partly also to amygdala and medial orbitofrontal cortex. From the primary auditory cortex (A1), the information propagates to belt and parabelt areas (Andrade and Bhattacharya, 2003). It is important to mention that auditory processing is not as straightforward as described, but processes are intertwined and happen in parallel. Especially noteworthy is that the auditory pathway does not only include bottom-up, but also top-down connections. (Koelsch, 2011)

First approaches of defining areas responsible for certain tasks in the brain assigned the right hemisphere to music processing and the left hemisphere to language processing. This belief is nowadays proven to be oversimplified. Music listening involves regions bilaterally throughout the brain, in the neocortex, paleo- and neocerebellum (Levitin and Tirovolas, 2009; Brattico et al., 2013). Lateralization does, however, play a role, as the auditory cortices in the two hemispheres are specialized. Temporal resolution is better in the left areas and spectral resolution in the right auditory

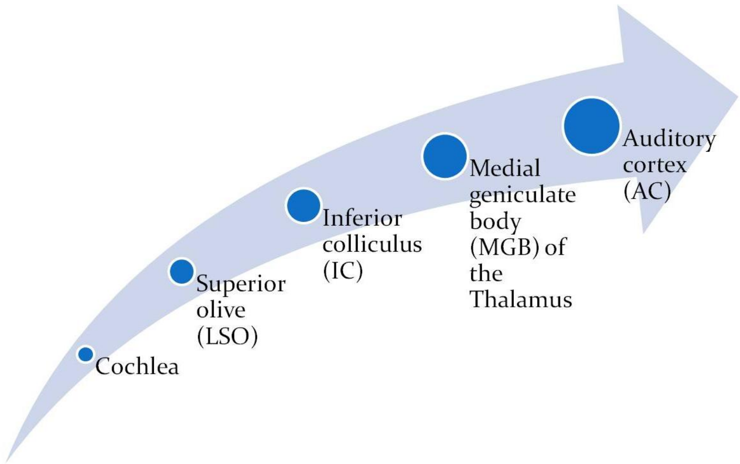



Figure 2: Auditory processing pathway in the brain.

cortex, which is thought to have developed due to the need to process acoustic information in both time and frequency domains (Zatorre et al., 2002).

Listening to music activates areas bilaterally throughout the brain which were located by fMRI studies. During attentive listening to music, the temporal (superior temporal gyrus), parietal (intraparietal sulcus), and frontal (precentral sulcus, inferior frontal sulcus and gyrus, and frontal operculum) areas are active (Janata et al., 2002b; see also Figure 1). Many areas that serve general functions, such as working memory, attention, semantic processing and target detection are also active during attending to music. Motor networks are coactivated during perception of music, which suggests a close link between the sensorimotor and auditory system (Zatorre et al., 2007). In an inter-subject correlation study with natural music stimuli, synchronization of brain areas has been revealed (Abrams et al., 2013). Of the subcortical auditory structures, the right inferior colliculus was synchronized across subjects. Moreover, the superior temporal cortex (from primary auditory cortex, Heschl's gyrus (HG), planum polare, planum temporale to posterior superior temporal gyrus (STG) in primary association cortex), fronto-parietal cortex (right inferior frontal gyrus, anterior angular gyrus and intraparietal sulcus) and motor cortex (premotor cortex, mid-cingulate cortex) showed synchronization across subjects. A determination of mean ISCs during listening to a naturalistic music stimulus in the analysis of Alluri et al. (2012) suggested significant correlations in large areas of the brain with the maximum in the auditory cortices.

Musical features are widely studied. The listener perceives different characteristic features, such as rhythm, loudness, timbre and pitch. It is possible to distinguish between different instruments (timbre), move head and body according to the tactus of the music (rhythm) and sing along known melodies (pitch). Many studies have identified distinct brain areas for one of those features (e.g., pitch and melody: Patterson et al., 2002; rhythm: Grahn and Brett, 2007; Grahn and Rowe, 2009; timbre: Menon, 2002). A more complex extraction of timbral, tonal and rhythmic features from music has been conducted by Alluri et al. (2012) who identified a network of cognitive, motor and limbic brain areas involved in processing of acoustic features of music. In another study, Alluri et al. (2013) extracted basic and complex acoustic features from music mixtures with and without lyrics and correlated them with the BOLD time courses to find their neural correlates. Dynamic aspects of music were analyzed in an MEG study by Popescu et al. (2004) and sound intensity in an electrocorticography (ECoG) study by Potes et al. (2012). Other musical attributes, like pleasure and anticipation are able to influence human emotions and well-being. Chanda and Levitin (2013) evaluated the notion that music improves health and well-being by activation of several neurochemical systems that are involved, e.g., in reward, motivation and pleasure. These three domains are connected to the mesolimbic striatal system (Zatorre and Salimpoor, 2013). The dorsal striatum was active during phases of anticipation and expectation, while the cerebral cortex and striatum were found to predict potential future events that contain a high reward (Zatorre and Salimpoor, 2013). With familiar music albums, expectancy was elicited by imagery of the following track on the album (Leaver et al., 2009). This 'anticipatory imagery' was connected to activity in the rostral prefrontal cortex and premotor areas, confirming enhanced fronto-striatal connections during anticipatory processing.

Listening to music involves processing and understanding the musical syntax of the song, e.g., principles and rules that are used in this context. The correlates of music-syntactic processing in the brain have been reviewed by Koelsch (2011). Involved in music-syntactic processing are pars opercularis of inferior frontal gyrus as well as the anterior part of STG and ventral premotor cortex (Koelsch et al., 2002). Parallel processing streams could be found for music-syntactic processing and language-syntactic processing, as well as in other hierarchical processes of syntactic information. The similar cognitive processing streams suggest that syntactic processing of music and language overlap at least partly (Koelsch, 2011). Other hints to shared neural processes of language and music were suggested by Carrus et al. (2011) who found possibly shared low-frequency oscillatory networks with EEG, and Fujioka et al. (2011) who confirmed that knowledge in speech and music is acquired culture-specifically in infants that are between 6 and 12 months old. For a review about the hierarchical processing of music and language, see Fitch and Martins (2014). Parallelism in processing was not only found for syntactic information in music and language, but is also evident in memory systems for melody and language. The connection is demonstrated in the overlap of the phonological loop of verbal working memory and the tonal loop for working memory for pitch in non-musicians (Koelsch et al., 2004; Peynircioğlu et al., 1998). In musicians, two working-memory systems could be identified: specific neural subcomponents of working memory are used only during verbal or only during tonal processing (Koelsch, 2011). Limited and controversial data is currently available about episodic and semantic musical memory. Semantic memory was proposed to be represented in the middle temporal gyrus and musical semantic representations in antero-temporal areas (Groussard et al., 2009, 2010); it was also connected to medial and orbitofrontal cortex, left angular gyrus and left anterior part of the middle temporal cortex (Platel, 2005).

These areas overlap only partly. In contrast to the semantic musical memory, the episodic musical memory is represented in middle and superior frontal gyrus and precuneus (Platel, 2005). Watanabe et al. (2008) showed that retrieval of musical information from long-term memory involves hippocampus and inferior frontal gyrus. Inferior frontal and temporal areas were also shown to be associated with recognition of familiar tunes (Jäncke, 2008). The rated attractiveness of a musical piece is strongly related to musical memory; it was proven that music plays an enormous role in building autobiographic memories (Eschrich et al., 2008).

The previously introduced findings have resulted mainly from fMRI studies. Music listening has been further investigated using EEG and MEG, e.g., by analyzing spontaneous oscillations in different frequency bands. A short summary will be given here and a more extensive review follows in Section 1.2.4. In 1991, a transient magnetic oscillatory response to auditory stimulation was found at ca. 40 Hz in the supratemporal auditory cortex (Pantev et al., 1991). Another rhythmic activity in MEG signals has been observed in the supratemporal auditory cortex for 8–10 Hz, and therefore it was suggested that each sensory modality has its own local rhythm (Tiihonen et al., 1991). The $\gamma$-frequency band has shown a special connection to music listening. Comparing musicians and non-musicians, the synchrony of the $\gamma$ band (>30 Hz) was increased in musicians over large cortical areas while listening to music (Bhattacharya et al., 2001; Bhattacharya and Petsche, 2001a,b). For other frequency bands it is not clear whether a connection to music itself can be identified or whether modulations rather appear due to the fact that tasks related to music undergo higher cognitive processing in the brain. However, modulations in the $\alpha$-band activity and increase in $\beta$ activity have been found in EEG, when subjects listened to self-chosen samples of music (Höller et al., 2012). The $\alpha$-band modulations have resulted from listening to subjectively relaxing and exciting music and increased $\beta$ activity has been found during listening to exciting music compared to rest.

### Musical Expertise

Musical training is a suitable model to study brain plasticity. Professional musicians have trained regularly for many years, mostly starting the training already early in life. Highly trained professional musicians and non-musicians have been compared often. Structural changes of the brain (anatomical) and differences in music processing (functional) have been found when comparing those two groups. Here, musical training is mostly regarded as instrumental musical training.

Anatomical differences have been found in different areas of the brain involved in musical processing. In the review of Herholz and Zatorre (2012), it is revealed that the auditory cortices of musicians consist of a greater volume, concentration, or thickness of grey matter, especially in the volume of HG. The HG was further investigated by Schneider et al. (2002), and large morphological differences were found between musicians and non-musicians in a 3D gray matter surface reconstruction (Figure 3). The volume of gray matter in the anteromedial HG was larger for

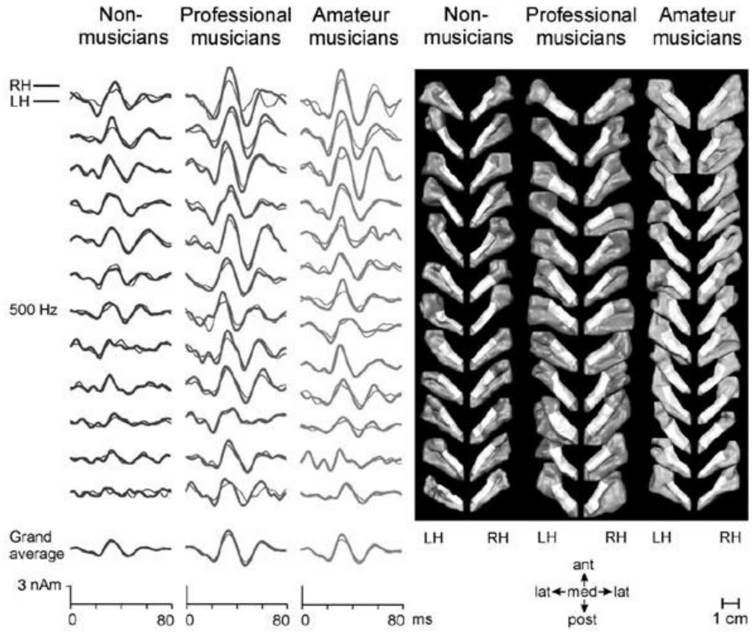



Figure 3: Auditory evoked signals (left) and 3D gray matter surface reconstructions of HG (right) for all subjects in the same order. Both the neurophysiological and the anatomical data show a large increase in professional musicians and a smaller increase in amateur musicians. (Adapted from Schneider et al., 2002)

musicians than for non-musicians. The amplitudes of neurophysiological responses to sinusoidal tones of different frequencies were strongly correlated with the gray matter volume as well as with the musical aptitude (Schneider et al., 2002). Finally, also the gray matter volume and musical aptitude showed a high correlation, meaning that highly trained musicians have a high gray matter volume in their anteromedial HG and therefore a different morphology of HG compared to non-musicians. Also motor areas, such as anterior corpus callosum, motor and premotor cortex and cerebellum, differ anatomically between musicians and non-musicians (Herholz and Zatorre, 2012). An increased size of the corpus callosum in musicians has been already found by Schlaug et al. (1995a). An anatomical asymmetry effect in musicians with absolute pitch, where the planum temporale is larger in the left hemisphere, has been shown by the same author (Schlaug et al., 1995b). In addition, the instrument of choice can effect the anatomical structure of the brain, as shown for keyboard versus string players, who showed gross-anatomical differences in the precentral gyrus (Schlaug et al., 2005). Altogether, these findings indicate that musicians show anatomical differences in several brain areas that are involved in auditory and motor processing.

Apart from differences in brain structure, many studies have been investigating functional changes in the brain due to musical training. Functional cortical reorganization resulting from instrumental training was found already in the 1990's by Pantev et al. (1998). In this study, musicians showed enlarged auditory evoked potentials in MEG measurements during listening to piano tones compared to pure tones. Another study by Pantev et al. (2001) confirmed those findings by comparing three groups of musical experienced subjects: Musicians with the ability to perceive absolute pitch, musicians with relative pitch and non-musicians who never played an instrument before. The auditory evoked field for piano tones in professional musicians with absolute pitch was strongest, followed by the musicians with relative pitch. The non-musicians group did not show a difference between responses for piano and pure tones. In EEG, event-related potentials have been used to investigate automatic, subconscious processing of repeated stimuli by measuring the mismatch between predicted and experienced acoustic stimuli. For example, in western harmonics, the last chord of a musical piece is very often expected by experienced musicians or music listeners. Musical experts were able to detect subtle harmonic incongruities in comparison to laymen (James et al., 2008). The brain response to a harmony rule violation was found to be higher in musical experts by Koelsch et al. (2002), and higher in folk musicians compared to non-musicians in the study of Brattico et al. (2013). In addition, differences in neurophysiological brain responses to simple musical sound violations have been found. The response to dissonant and mistuned chords was stronger in musicians than in non-musicians (Brattico et al., 2009). Furthermore, long-term musical training leads to a higher memory capacity for complex tone patterns, as shown in the study of Boh et al. (2011). Kuchenbuch et al. (2012) found an earlier response to musical sound violation in musicians, especially in the left hemisphere. Later, Kuchenbuch et al. (2014) investigated the influence of musical training in more detail and suggested an enhanced higher-order processing of music stimuli in trained participants. Bottom-up sensory processing was less modulated by expertise whereas stronger top-down modulation of multisensory expectancies occurred due to musical training. Source localization of the mentioned studies of simple sound-violation responses have located the origin in the supratemporal plain of the temporal lobe and partly in the frontal cortex. These findings imply that musical training reshapes neuronal populations in the auditory cortex so that they automatically detect subtle changes in auditory paradigms (Münte et al., 2002). Changes in the neuronal populations do not only depend on musical training in general, but for musicians it has been found that their specific instrument changes the way of processing music in the brain. Pantev et al. (2001) has investigated the change in cerebral representations of frequently used fingers for different instruments. In this context, it was found that especially for the fifth finger in string players the representation in the somatosensory cortex was enlarged, also correlated with the age of onset of musical practice. Another instrument-specific finding has been reported by Shahin et al. (2008). The induced $\gamma$-band activity was enhanced in musicians specific to their instrument of practice (timbre). Furthermore, experience-specific networks in auditory areas were found in a study of Margulis et al. (2009) comparing players of different instruments. Sensitive areas in the auditory association cortex and activation of sound-motor interactions (precentral gyrus) were found whilst listening to music played with the own instrument, but not with another instrument. For instrumental training, especially the sensorimotor input influences the response in auditory areas. It is assumed that this happens via the strong interactions between auditory and motor areas (Zatorre et al., 2007) and also via the frequent use of motor skill learning pathways. Thus, many of these studies confirm that with instrumental training, music does not only activate auditory areas responding to musical stimuli, but also a network of motor areas. Sensorimotor representations differ depending on the instrument that a musician plays. Involving more than one sensory area in musical training has shown beneficial effects. Multimodal sensorimotor-auditory training was shown to induce more plastic changes in the auditory cortex of non-musician subjects than auditory training alone (Pantev et al., 2009). Plastic changes occur especially during sensitive time windows in early phases of human development (Rauschecker, 2001), which makes it easier to learn a musical instrument during this time. It is, however, still possible to induce plasticity in later years, as was shown by Trainor et al. (2003), where adult non-musicians showed similar, but weaker effects for the same cortical responses after receiving musical training.

Not only auditory and somatosensory systems are connected with musical training. Herdener et al. (2010) examined the hippocampus, comparing various forms of novelty detection in sound patterns, as they are known to be processed in this area. In professional musicians, the hippocampal area showed enhanced activity compared to musical laypersons, giving evidence that hippocampus undergoes functional changes connected to musical training in humans. In addition, neurophysiological studies associated the $\gamma$-frequency band with music listening. The synchrony in the $\gamma$ band was significantly higher in musicians than in non-musicians (Bhattacharya et al., 2001; Bhattacharya and Petsche, 2001a). Another study investigated connectivity in the brain depending on musical expertise. Increased local connectivity has been found in areas that are involved in higher-order auditory processing, working and semantic memory processes. Absolute-pitch musicians showed a high local connectivity in peri-sylvian language areas; planum temporale, planum polare, Heschl's gyrus, lateral aspect of the superior temporal gyrus, superior temporal sulcus (STS), pars triangularis, and pars opercularis were hub regions (Jäncke et al., 2012).

To summarize, the neural correlates of music have been investigated in cognitive brain research for many years. The influence of musical expertise has been and is an important aspect. Using complex stimuli like entire songs is a relatively new approach to study the neural correlates of music listening. Perception of music during listening to real music can give new insights about the higher-order processing of complex natural stimuli. In this study, the brain synchronization between subjects during this process is investigated by analyzing the finegrained spectrotemporal neural dynamics. Additionally, the influence of the type of music reflected in three selected genres is evaluated. Musical expertise has been proven a valuable example of plasticity in the brain. Another aspect of this thesis is therefore to validate how musical training and expertise affect the neural dynamics during music listening.

Background about the chosen method to study music perception is given in the next section (1.2.2) and basic knowledge about viable analysis approaches in the following sections (1.2.3-1.2.5).

### 1.2.2 Magnetoencephalography (MEG)

#### Neural Basis of MEG Signal Generation

Magnetoencephalography is a non-invasive brain imaging method that directly measures the weak magnetic fields due to the electric currents in active neuron populations in the brain. For studying music processing, this method holds several advantages. Firstly, it is a non-invasive brain imaging method which does not interfere with the human body. In addition, this direct measurement of neuronal activity increases the understanding about communication between neurons in the brain. The major benefit of MEG is the high temporal accuracy which allows to follow fast musical events that are evolving in time. This excellent temporal resolution is not reached by BOLD fMRI which measures comparably slow changes in blood oxygenation.

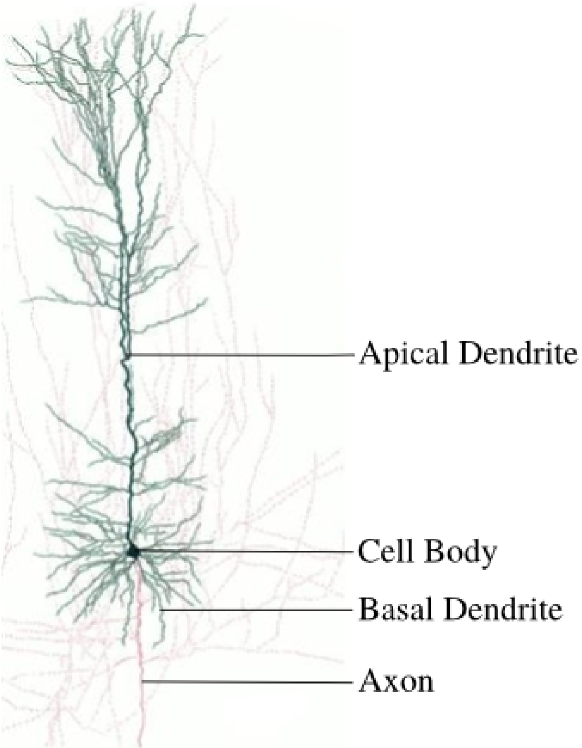
Neurons consist of a neural cell body, in which all maintenance functions take place; an axon, which conducts the electrical signals away from the cell body towards other neurons or muscles; and dendrites, which are connected to other neurons and are responsible for transporting incoming information to the cell body (Figure 4a). Synapses connect the axon terminals to dendrites or motor end plates of muscle fibers and are a crucial factor in neural signaling in terms of forwarding electrical signals (action potentials) that arise from sensory stimulation throughout the neural network in the brain.

The magnetic fields measurable by MEG are due to synchronous, postsynaptic, intracellular currents derived mainly from pyramidal neurons of the cerebral cortex (Hari, 1990). The parallel orientation of the apical dendrites of pyramidal neurons leads to a spatial summation of the signals (Figure 4b). In theory, the activation of one synapse in a thousand could produce a detectable signal. However, due to partial cancellations of the electromagnetic fields that occur because of oppositely directed source current flows in close cortical regions, an activation of a larger area is still necessary for a detectable signal (Hämäläinen et al., 1993).

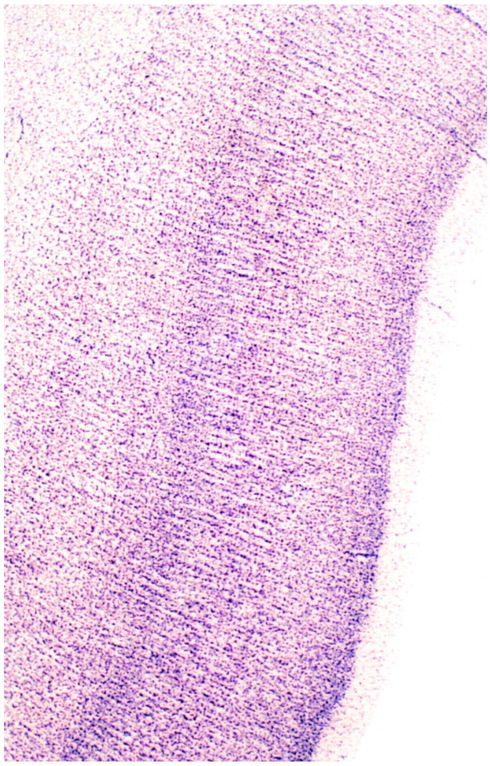
Additionally, temporal summation occurs in slow, dipolar postsynaptic currents, whereas action potentials show only little temporal summation and are therefore not directly detected (e.g., Lopes da Silva, 2010).

#### Requirements to Measure Magnetic Signals from the Brain

The level of magnetic signal produced in the human brain compared to external magnetic fields is very low. For example, the Earth's magnetic field is 8-9 orders of magnitude (one billion times) stronger, and magnetic noises from surrounding laboratory equipment and moving magnetic objects are 1000 times stronger. For comparison of other sources, see Figure 5. (Parkkonen, 2010)




(a) Simplified structure of a pyramidal neuron. (Adapted from Mel, 2007)



(b) Parallel orientation of neurons in the superior temporal sulcus of a human brain ($\times 40$). Nissl-stain. (Adapted from Jones, 2000)

Figure 4: Pyramidal neurons. Schematic structure of a pyramidal neuron (a) and orientation of pyramidal neurons in the human brain (b)

For this reason, to pick up the weak magnetic brain signals, several prerequisites have to be fulfilled:

1. *Magnetically shielded room*
   The MEG device has to be placed in a room that is shielded from external magnetic fields to cancel high-magnitude magnetic interference. The shield consists of layers of mu-metal and aluminium which guide the external fields around the shielded room.

2. *Magnetically clean subject and measurement environment*
   It has to be ensured that no magnetic objects are present during the measurement in the shielded room. Therefore, the subject has to remove magnetic clothes and metal on the body. In case of magnetic metal inside the body, the subject has to be excluded from MEG measurements. Furthermore, all devices used during a measurement have to be tested for MEG-suitability (i.e., they must not produce magnetic interference).

3. *Use of sensors with exquisite sensitivity*
   SQUID (Superconducting Quantum Interference Device) sensors were first

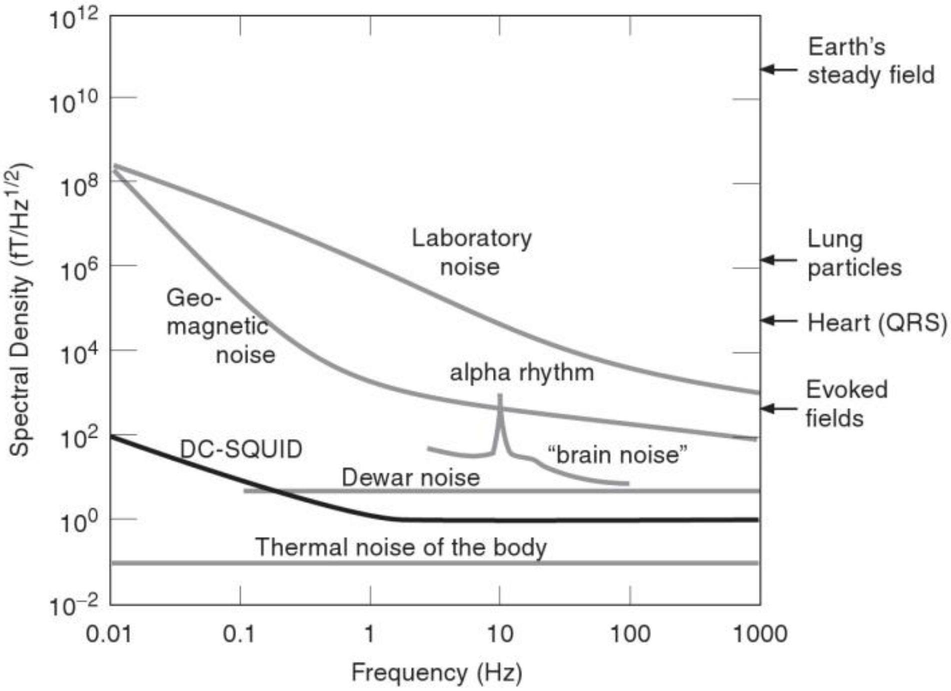



Figure 5: Different magnetic field sources and their strength. (Adapted from Hämäläinen et al., 1993)

used in MEG by David Cohen (1972). With a one-channel SQUID sensor he was able to measure neuromagnetic signal, without electric reference, for the first time. To reach the superconducting state, SQUID sensors are cooled by liquid Helium at $-269°$. Nowadays neuromagnetometers house hundreds of SQUIDs covering the whole scalp that are able to pick up concerted action of cortical neurons (Hari and Salmelin, 2012). For a more detailed insight in MEG instrumentation, consult Chapter 2 of Hansen et al. (2010).

After the measurement, artifact- and noise-removal algorithms can be applied to the data. The signal space separation (SSS) method decomposes the data to signals that originate from brain sources (inside) and external interferences (outside) by Maxwell equations and removes the outside contribution from the raw data (Taulu et al., 2004; Taulu and Kajola, 2005; Parkkonen, 2010). The signal space projection (SSP) method projects out signal patterns identified as interference and thereby cleans the signal from those (Uusitalo and Ilmoniemi, 1997; Parkkonen et al., 1999).

### Inverse Problem and Source Modeling

The neuromagnetic forward problem is to calculate the electric and magnetic signals from a given primary current distribution in the brain, which is solvable uniquely. The inverse problem is to map primary currents from observations of magnetic fields outside of the skull; the solution to this problem is not unique. The measured data can be expressed as a discretized model

$$\mathbf{y} = \mathbf{G}\mathbf{q} + \mathbf{e}. \tag{1}$$

Vector $\mathbf{y}$ contains the measured magnetic field components at the magnetometers, $\mathbf{G}$ is the gain matrix, 'lead field matrix' or forward operator that gives the measured signals when multiplied with the primary currents $\mathbf{q}$, which is a vector containing the dipole amplitudes at each source point, and $\mathbf{e}$ is observation noise. (Hämäläinen et al., 1993)

One of the computational challenges is the existence of silent currents. MEG is highly sensitive to tangential currents (Lopes da Silva, 2010), but due to magnetic characteristics, primary currents oriented radial to the skull are invisible to MEG sensors. In contrast to MEG, with EEG it is possible to pick up both tangential and radial currents. However, the skull and scalp create major distortions of electric fields in EEG measurements, which is not the case for MEG, as the skull is magnetically transparent (Hari and Salmelin, 2012). The problem of silent currents manifests $\mathbf{L}$ as a non-trivial null space of $\mathbf{G}$ in Equation 1. To choose a physiologically meaningful solution from all possible solutions, it is necessary to include prior information concerning the primary currents. (e.g., Somersalo, 2007)

One way to add constraints is the L2 minimum-norm estimation (Hämäläinen and Ilmoniemi, 1994). Minimum-norm solutions distribute a large number of elementary sources (dipoles) throughout the cortex. Constraints for the distribution contain individual head geometries and cortical anatomies from the anatomical MRIs of participants and therefore increase the spatial resolution of MEG (Hari and Salmelin, 2012). To determine the dipole amplitudes and their time courses, the norm of dipole moments $\mathbf{q}$ across the cortically constrained source points has to be minimized. The L2 minimum-norm estimation finds an optimal solution $\hat{\mathbf{q}}$ by minimizing the least-squares error between the measurement and the model data by adjusting the dipole orientations and amplitudes:

$$\hat{\mathbf{q}} = \underset{\mathbf{q}}{\operatorname{argmin}}(||\mathbf{y} - \mathbf{G}\mathbf{q}||^2 + \lambda^2||\mathbf{q}||^2), \tag{2}$$

where $\lambda$ is the regularization coefficient. If the solution is formulated inside the Bayesian framework and if the noise covariance matrix $\mathbf{C}$ and source variance matrix $\mathbf{R}$ are available, the L2 minimum-norm estimate can be written as:

$$\hat{\mathbf{q}} = \mathbf{R}\mathbf{G}^T(\mathbf{G}\mathbf{R}\mathbf{G}^T + \lambda^2\mathbf{C})^{-1}\mathbf{y}. \tag{3}$$

(Hämäläinen et al., 2010)

Often depth weighting is included as an additional factor to account for the bias towards superficial currents with this method.

A suitable conductor model has to be chosen for calculating the forward solution. It is possible to use a spherical volume conductor as the head can be nearly accounted for as a sphere. The boundary element model (BEM), however, accounts better for the realistic head geometry. The inner skull surface is used in the single-compartment boundary element model. The benefits and influences on forward solutions of different conductor models has been investigated by, e.g., Stenroos et al. (2014).

Despite effortful trials to solve the magnetic inverse problem, the spatial resolution of MEG remains low compared to functional MRI and therefore barriers towards precise, non-invasive localization of electrophysiological brain activity exist.

### 1.2.3 Inter-subject Correlation

> "Individual brains 'tick together' ... when exposed to the same environment." (Hasson et al., 2004)

Uri Hasson introduced the method of inter-subject correlation (ISC) for the 'environment' of movie stimuli (Hasson et al., 2004). ISC is a model-free analysis method to detect common stimulus-driven brain activity that is temporally synchronized between subjects; it is not a measure of activity *per se*. ISC does not require *a priori* knowledge about the stimuli, and is therefore an alternative, data-driven analysis approach. Since its introduction in 2004, it has been used frequently to analyze fMRI data, where the ISCs are calculated as voxel-wise correlations of brain activity between subjects (Abrams et al., 2013). Especially visuoauditory movie stimuli have been investigated using ISC (Hasson et al., 2004, 2008; Golland et al., 2007; Jääskeläinen et al., 2008; Kauppi et al., 2010). Furthermore, narratives (Wilson et al., 2008) and music (Abrams et al., 2013; Alluri et al., 2013) have been used to determine synchronized brain activity. For movie stimuli, Hasson et al. (2008) found that correlations of brain activity between subjects can be connected with subsequent memory encoding of the observed clip. Moreover, Nummenmaa et al. (2012) found that brain areas synchronize between subjects that share emotions elicited by movie excerpts.

In a review, Hasson et al. (2010) summarized previous fMRI inter-subject synchronization findings using natural stimuli, e.g., movies and narratives. Despite the usage of complex stimuli in an uncontrolled task (free viewing and/or listening), some stimuli evoked reliable brain activity between subjects; see Figure 6.

Inter-subject correlation has been found to be a viable approach, especially when utilizing complex, natural stimuli. Information integration over a long period of time in cognitive processes can be examined. Replacing artificial stimuli with complex, real-world stimuli can be beneficial to learn more about the processing of those stimuli. The ISC approach has also been found suitable for music studies, because of the manifestation of structural elements, gestalt and integration of information over extended time periods (Abrams et al., 2013). The reliability and reproducibility of

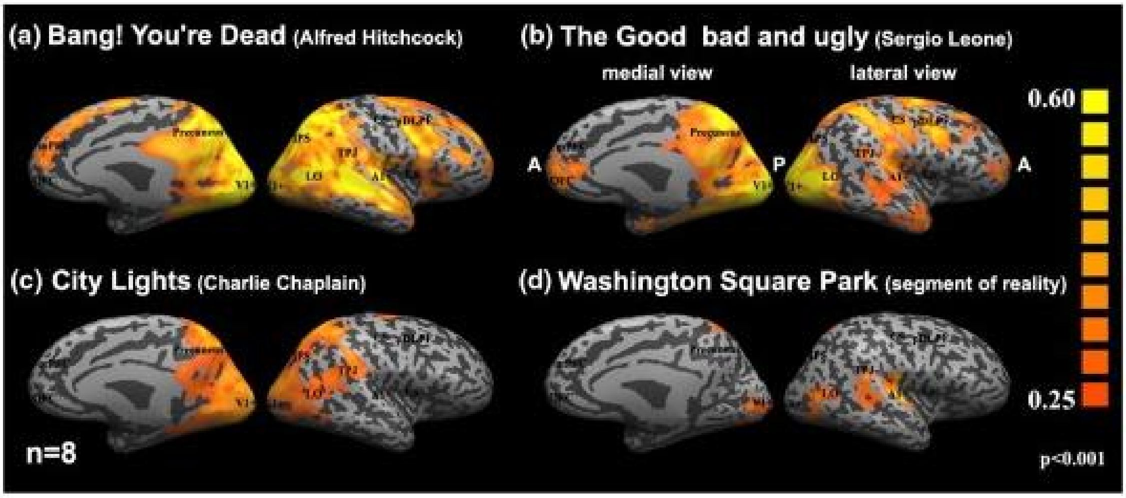



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Figure 6: Inter-subject correlation (ISC) of brain responses to four different movies. Shown are medial and lateral views of 'inflated' right hemisphere. Edited movies (Hitchcock, Leone and Chaplin) evoked greater and more extensive ISC than the real-life, unedited video. The range of ISC values is visualized in a color spectrum ranging from dark orange ($r = 0.25$) to yellow ($r = 0.60$. (Adapted from Hasson et al., 2010)

neuronal responses was found to be enhanced for naturalistic stimulation compared to artificial stimulation, as introduced in Hasson et al. (2010).

As viable as ISC has been proven to be for complex stimulation in fMRI, it has rarely been used in MEG studies. The methodology of deriving ISC from MEG data has not been standardized. However, Lankinen et al. (2014) analyzed single-trial MEG data from subjects watching a silent movie. A spatial filtering model was applied and its parameter values were estimated by using multi-set canonical correlation analysis (M-CCA). The time courses were correlated with minimum-norm source current estimates (MNEs) to visualize the ISC. The findings confirmed and extended previously discussed ISCs during movie viewing in fMRI studies. Moreover, a linear correlation approach has been applied to the same data set by Suppanen (2014). The correlations were calculated in source space from MNE-derived time courses across subjects. Again, the results confirmed previously found synchronously active areas in the brain across subjects and added new temporally sensitive information. The results of both studies suggest that ISC is a viable approach to analyze also MEG data.

### 1.2.4 Oscillatory Activity with Auditory Stimuli

Spontaneous oscillatory activity in the cortex is modulated by stimuli and tasks (Hari and Salmelin, 1997). The occipital $\alpha$ rhythm (8–13 Hz), for example, was the first spontaneous brain rhythm ever measured (Berger, 1929) and it is modulated, e.g., by the opening and closing of the eyes. Another well-known oscillation is the $\mu$

rhythm (8–13 Hz), recorded over the rolandic regions (Gastaut, 1952). This section will concentrate on oscillatory activity modulated by auditory stimulation.

The phase pattern of $\theta$-band (4–8 Hz) responses recorded from the auditory cortex has been found to track and discriminate spoken sentences (Luo and Poeppel, 2007). Another language-related study showed that low-frequency oscillatory networks ($\delta$ (1–4 Hz) and $\theta$) get activated during the syntactic processing of music and language, indicating the networks might be shared (Carrus et al., 2011). A specific 'idling' rhythm has been found in the human temporal cortex: the 10-Hz oscillation, later named $\tau$ ('tau') rhythm, was detected by Tiihonen et al. (1991) in the supratemporal auditory cortex and later confirmed by Lehtelä et al. (1997). The rhythm was suppressed in the majority of subjects by auditory input. The $\alpha$ band was investigated in an EEG network study by Wu et al. (2013); during music listening the $\alpha$-band synchronization was enhanced.

In the $\gamma$ band (25–90 Hz), a transient magnetic oscillatory response originating in the supratemporal cortex has been identified at ca. 40 Hz by Pantev et al. (1991). In EEG, long-range synchrony in the same band was found whilst listening to music (Bhattacharya et al., 2001). Furthermore, timbre-specific activity in the $\gamma$ band has been identified related to musical training of different instruments (different timbres; Shahin et al., 2008). More generally, $\gamma$ oscillations have been found to play a role in higher-order auditory processing in speech and music (Lachaux et al., 2007). Also Trainor et al. (2009) confirmed the involvement of $\gamma$-band activity in attention, expectation, memory retrieval and integration of multisensory processes. Here, the influence of musical training was investigated, and the results suggest that musical training affects oscillatory networks associated with executive functions. In more recent studies, it has been suggested that $\gamma$-band variations are highly comparable with hemodynamic responses as measured in BOLD fMRI (e.g., Kaiser and Lutzenberger, 2003; Kunii et al., 2013; Zumer et al., 2010).

### 1.2.5 The MEG Band-limited Power (Envelope)

Different MEG frequency bands have been investigated by computing the time-varying envelope of band-bass filtered signals ('band-limited power'). This approach has been introduced by Salmelin and Hari (1994) as 'temporal spectral evolution' (TSE), and has been used to characterize oscillatory activity in specific frequency bands. The exact procedure will be explained in more detail in Section 2.5.

The method allows to compare the resulting band-limited power time series with the BOLD time series in fMRI paradigms. The approach has been widely applied in functional connectivity studies, especially to investigate MEG resting networks and to compare found networks to known ones from functional imaging studies (de Pasquale et al., 2010; Shmuel and Leopold, 2008; Brookes et al., 2011). It was suggested that a correlation between neuronal activity and BOLD signals exist, proven strongest for the $\gamma$ band (e.g., Shmuel and Leopold, 2008). Furthermore, the resting networks in MEG reveal a synchronous modulation of band-limited power in $\theta, \alpha$ and $\beta$ bands (de Pasquale et al., 2010). A $\beta$-band-limited power decrease appears negatively correlated with the BOLD signal change (Brookes et al., 2011).

Other studies using MEG power envelopes have investigated, e.g., functional connectivity during movie watching (Betti et al., 2013), different phases of sleep and wakefulness (He et al., 2008; Nir et al., 2008; Liu et al., 2010) and before and after using acupuncture (You et al., 2012).

Inter-subject correlation of envelopes of different frequency bands has been used previously by Suppanen (2014) for movie stimuli.

## 1.3 Hypothesis

Measuring responses to continuous natural stimuli with MEG is a relatively new approach. Using complex real-world stimuli, the inter-subject correlation would be a feasible way to uncover the responding brain areas. In contrast to previously used free-viewing movie stimuli, free-listening music stimuli of three songs will be compared. The main hypothesis is that the MEG ISC findings will confirm previously found active areas in the brain (in different frequency bands) during music listening. These areas include temporal (HG, planum polare, planum temporale, auditory association areas, especially STG), fronto-parietal (intraparietal sulcus, precentral sulcus, inferior frontal sulcus and gyrus, pars opercularis), motor (premotor cortex, mid-cingulate cortex) and emotion-related regions (left anterior cingulate, insula, parahippocampal gyrus). Comparing subjects with different levels of expertise, the same areas (especially in planum temporale, planum polare, Heschl's gyrus, STG and STS) and additional areas including motor areas, pars triangularis and pars opercularis are expected to show a higher synchrony in musicians compared to non-musicians.

# 2 Methods

## 2.1 Participants

Forty-five healthy individuals (21 females, 22 males; mean age 28.3±8.9; 2 left-handed) with normal hearing capacity and no history of neurological diseases participated in the study. They were grouped into 26 'musicians' and 19 'non-musicians'. A musician had to have undergone professional musical education, e.g., in Sibelius Academy of Music in Helsinki, or other long-term musical education. Participants were non-musician in case of no formal music education (amateur) and if they had never played an instrument.

Two data sets of musician subjects were excluded from the analysis in the above subject counts. One was found amusic in both MBEA (Montreal Battery of Evaluation of Amusia) and Seashore tests[1] and moved considerably during data acquisition. The other subject was diagnosed with a hippocampal lesion and therefore could not be considered healthy.

Informed consent was received prior to the recordings from each subject according to guidelines of BioMag Laboratory, Meilahti, Helsinki and Advanced Magnetic Imaging (AMI) Centre, Otaniemi, Espoo. The experimental procedures were approved by the Ethics Committee of University of Helsinki and Helsinki University Central Hospital.

This thesis investigates a subset of participants of a combined MEG/EEG/fMRI study that includes a larger number of subjects.

## 2.2 Data Acquisition

The neuronal activity of the brain was recorded in BioMag Laboratory in Helsinki University Central Hospital using a 306-channel (Elekta Oy, Helsinki, Finland) whole-head MEG system (sampling rate 600.615 Hz and pass-band 0.1–172.2 Hz). Additionally, EEG was recorded with a 60-channel system (Easycap, Herrsching, Germany) with caps selected according to the head size and built for simultaneous EEG and MEG recordings. Prior to the measurement, the positions of four marker coils and EEG electrodes were determined by digitizing them in relation to the nasion and both preauricular points with an Isotrak 3D-digitizer (Polhemus Inc., Colchester, USA). The head position with respect to the magnetometer was measured before each data acquisition. Vertical and horizontal electrooculograms (EOG) were recorded. The EEG reference and ground electrodes were attached to the nose and cheek, respectively. For noise-covariance computation, empty-room data (without a subject present) was acquired for ∼10 min. The anatomical T1-weighted images (MPRAGE) were acquired on a 3 T MAGNETOM Skyra whole-

[1] These two tests evaluate music processing and musical ability.

body MRI scanner (Siemens Healthcare, Erlangen, Germany) at AMI centre in Aalto University and checked for incidental findings by a physician.

Three songs belonging to different genres (Figure 7) were used as stimuli. The stimuli were presented at a comfortable noise level by Presentation Software (Neurobehavioural Systems Ltd., Berkeley, CA, USA) through plastic tubes and silicon earphones. Subjects were instructed to sit in an upright position, keep the head still and listen to the music. The three musical pieces were played in a random order with short pauses between the pieces. The modifications done to adjust the pieces to the experiment are summarized in Table 1. Furthermore, the resting state was recorded for 5–10 min. The task was to sit in the same position and keep the eyes open.

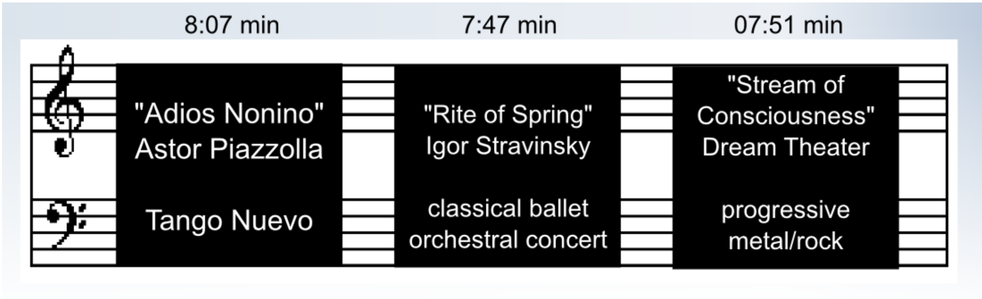



Figure 7: Three whole, real musical pieces of different genres (title, composer/performer, genre) were presented at a comfortable noise level to the participants. Subjects were instructed to keep the head still and listen to the stimuli.

Table 1: Modifications to the music stimuli.

| *Stimulus* | *Modifications* |
|---|---|
| ‘Adios Nonino’ | shortened |
| ‘Rite of Spring’, ‘Le Sacre du printemps’ | excerpt of Part I, shortened |
| ‘Stream of Consciousness’ | shortened |

A variety of psychological and behavioral questionnaires evaluating the general mental background and acquisition of musical expertise were filled by subjects prior to the experiment. After the experiment, they were asked to continuously rate the music pieces again in terms of arousal, pleasure, expectancy and beauty. Three liked and disliked songs were listed additionally. Blood samples were taken for genetic analysis. The analysis of these data is not included in this thesis.

## 2.3 Data Preprocessing

For the removal of external magnetic interference, the signal space separation (SSS) method (Taulu et al., 2004) was applied by MaxFilter software version 2.2.10 (Elekta Oy, Helsinki, Finland). Prior to SSS, bad channels had been identified and marked manually by the function *mark_bad_fiff* of Elekta Neuromag software. The MaxFilter default values were used for further bad channel detection and the *autobad* option was set to scan through the first 60 data buffers. The fine-calibration and cross-talk compensation measurements needed by MaxFilter were carried out in BioMag Laboratory in 2012.

Artifacts due to cardiac activity, eye movements and eye blinks were suppressed by the signal space projection (SSP) method in MNE Python (Hämäläinen, 1995; Jousmäki and Hari, 1996; Nolte and Curio, 1999; Tesche et al., 1995; Uusitalo and Ilmoniemi, 1997). Rejection parameters were chosen as summarized in Table 2. For the cardiac rhythm detection, channel 'MEG 143' showed the most prominent cardiac activity. The artifact was averaged over all MEG channels and the SSP created by principal component analysis. Both EOG channels ('EOG 061' and 'EOG 062') were used to create the projector for eye blinks and movements. As a control step we decided to apply the generated SSP operators to averaged evoked MEG data of selected participants with MNE (Gramfort et al., 2013). The results showed that the neural signal is not altered by the SSP operator, meaning that the operator only removes artifacts that can be interpreted as noise.

The MEG noise covariance matrix was calculated from empty-room data for the MNE inverse operator. Therefore, the data were processed in the same way as the raw MEG data (SSS applied) and additionally a pass-band filter of 0.1–90 Hz was applied. For EEG, the average of the diagonal elements of the noise covariance matrix from a resting state recording with eyes open was calculated. The two joined matrices made up the full noise covariance matrix.

Table 2: Rejection parameters for SSP.

| *Source* | *Rejection for values higher than* |
|---|---|
| gradiometers | $3000\,\mathrm{fT\,cm^{-1}}$ |
| magnetometers | $5000\,\mathrm{fT}$ |
| EEG | $100\,\mu\mathrm{V}$ |

## 2.4 Setup of Source Space and Minimum-norm Source Current Estimates (MNEs)

In order to calculate the MEG minimum-norm source current estimates, the MNE Suite software package[2] described by Gramfort et al. (2013) was utilized. The anatomical MRI data were used for a reconstruction of the cortical surfaces by FreeSurfer[3] (Dale et al., 1999; Fischl et al., 1999a,b) software. The processing steps included transformation to Talairach coordinates, skull stripping (Segonne et al., 2004), segmentation of white and grey matter volumetric structures (Fischl et al.,

[2]MNE, Martinos Center for Biomedical Imaging, `http://martinos.org/mne/stable/`
[3]FreeSurfer, Martinos Center for Biomedical Imaging, `http://freesurfer.net/`

2002, 2004), intensity normalization (Sled et al., 1998) and inflation of both hemispheres (Fischl et al., 1999a).

With the help of MNE suite, the source space was set up with an octahedral surface with 4098 sources per hemisphere and 4.9-mm source spacing. The watershed algorithm of FreeSurfer (Segonne et al., 2004) was used for setting up the surfaces for the boundary element model (BEM). However, the watershed parameters had to be changed individually for each subject. The normalized brainmask output (*norm.mgz*) of FreeSurfer was used for the majority of subjects in order to overcome field inhomogeneities shown in the T1-weighted image. Manual editing of the brainmask (*brainmask.mgz*) or the normalized brainmask was necessary to improve the skull-strip in individual cases to ensure a regular BEM. The forward model was set up with 5120 triangles per hemisphere.

For the construction of the forward and inverse operators, the MEG and MRI data were coregistered in Mrilab[4] utilizing the digitized positions of the three anatomical landmarks, the nasion and two preauricular landmarks, and the four MEG marker coils and EEG electrodes. Those digitized points were imported to Mrilab and overlaid on the T1-weighted anatomical image. The MEG-MRI coordinate transformation was adjusted (translation and in rare cases rotation) to align the digitized data to the surface of the scalp.

The forward operator was calculated with MNE under consideration of the MEG preprocessed data file, BEM, MEG-MRI coregistration and forward solution. For the inverse operator, the forward solution and noise covariance matrix were used as well as a loose orientation constraint (with transverse component weight 0.2) and depth weighting.

## 2.5 Inter-subject Correlation Analysis

The inter-subject correlation (ISC) analysis for MEG data has been performed for an MEG movie data set (Lankinen et al., 2014) earlier by Suppanen (2014). The same analysis method and implementation for the continuous music listening data was used in this study. Figure 8 shows an overview of the analysis steps.

The method is analogous to ISC methods for fMRI data and therefore comparable to voxel-wise between-subjects comparisons in fMRI studies. It calculates the ISC between homologous source points located in common space. First, the band-limited signals of the preprocessed MEG data were band-pass filtered into selected frequency bands ($\theta$: 4–8 Hz, $\alpha$: 8–12 Hz and $\beta$: 12–25 Hz) using the Butterworth filter implemented in Matlab2013b.

The envelopes (Salmelin and Hari, 1994) of the band-limited signal were computed by taking the absolute value of the Hilbert transformed (Matlab function: *hilbert*) signal in the source space. A 4-Hz low-pass filter was applied to downsample the

[4] Mrilab, Elekta Oy, Version 1.7.25, 2008.

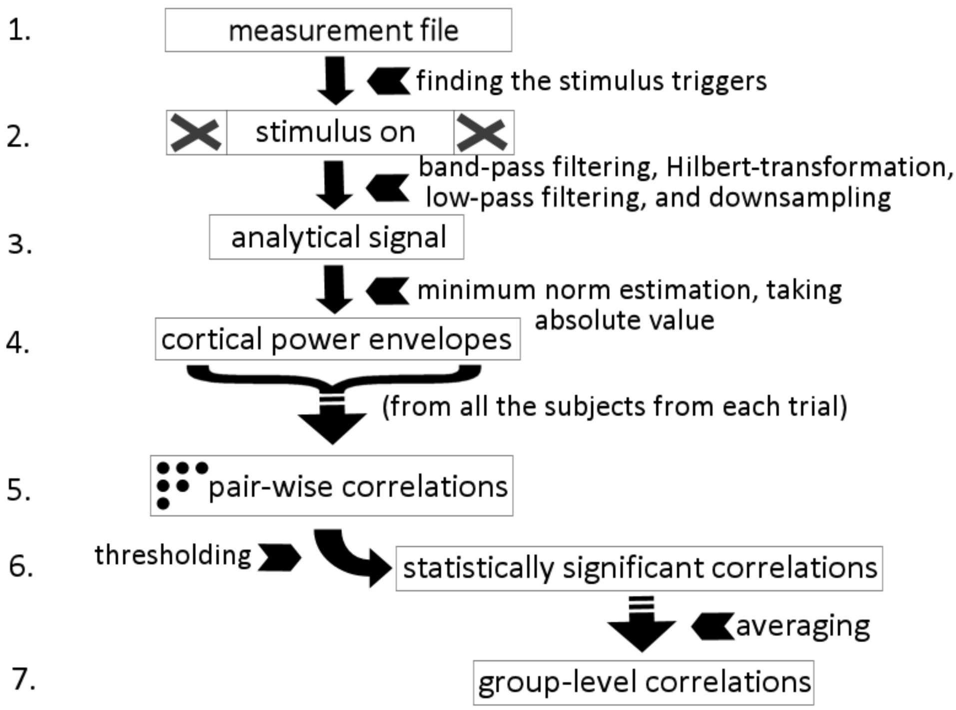



Figure 8: Simplified diagram of the Matlab-modules comprising the ISC analysis. The block structure allows fast changes without recomputing previous steps. (Adapted from Suppanen, 2014)

envelope signal to 10 Hz. The resulting subject-wise cortical power envelopes were morphed into the source space of FreeSurfer's average subject 'fsaverage'. The morphgrade '5' was used, and 10242 vertices per hemisphere were obtained by the MNE morph function *mne_make_movie*. The resulting identical number of vertices in all subjects in the average source space enabled the correlation and group-average computations.

In preparation for the inter-subject correlation analysis, the exact duration of the music stimulus was determined by finding the start and end triggers for each musical piece. Every start point was marked in the trigger channel, but trigger points marking the end of the music stimulus were only present for five subjects. The mean time of the duration of those five subjects was added to the start trigger time point for the remaining subjects. For the resting-state recordings, the start trigger was at the beginning of the recording and the end trigger was set at 4.8 min according to the shortest rest recording. Two subjects had to be excluded from computing resting state ISCs due to missing and excessively noisy rest recordings.

Temporal correlations for the three music pieces and the resting-state recordings were computed between the envelopes at the corresponding source points for each subject pair. The correlation coefficients were computed as inner products of normalized vectors, as by Suppanen (2014), to accelerate the computation. The significance of the correlations was evaluated by $t$-test to inspect the deviation of correlation means from zero. Only values with a significance level $p < 0.05/2$ were accepted.

The correlations were calculated using 20-s temporal windows. The total correlation over time was assessed by averaging those windows. Calculating each pair-wise correlation between subjects in an independent trial resulted in >10000 subject pairs in total, which were then averaged for different subgroups of subjects to get one ISC statistic per group. Groups were defined as follows: (1) ISC over all subjects, (2) musicians and (3) non-musicians. The average ISC is computed as

$$\bar{r} = \frac{1}{\frac{m^2 - m*2+1}{2}} \sum_{i=1}^{m} \sum_{j=2, j>i, j \neq i+n}^{m} r_{ij}, \tag{4}$$

where $m$ is the number of independent trials and $n$ is the number of subjects included in the group average. The group average over all pair-wise correlations $\bar{r}$ was visualized as an overlay in the 'fsaverage' source space using the MNE Suite software package.

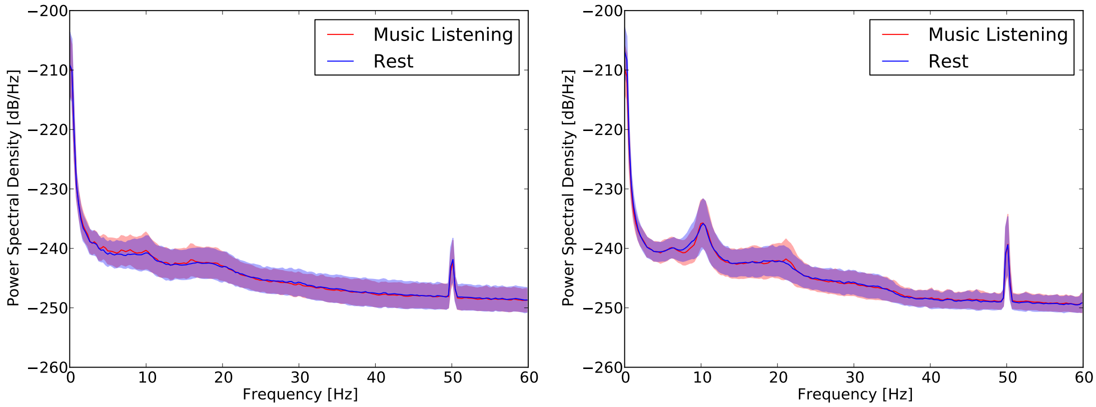
The Matlab-based script from Suppanen (2014) was utilized after adapting it to this dataset. The methodology of computing the ISC was kept exactly the same.

# 3 Results

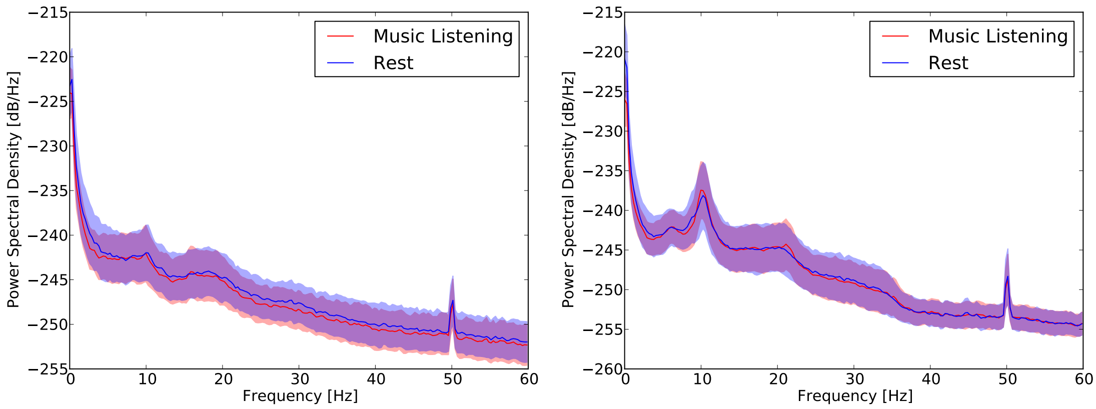
## 3.1 Power Spectral Density Analysis

To examine the variation of signals in the raw MEG signal and in the source-projected power envelopes, the power spectral density was computed for both cases.

The power spectra of the raw data are visualized for the frequency range of 0–60 Hz (Figure 9) before and after preprocessing. Preprocessing included signal space separation and signal space projection to remove external interference and eye-blink as well as heart-beat artifacts. The music-listening and rest conditions show only slight variations, but rather follow a similar distribution for the two selected musicians. Peaks in the raw spectral density are visible at 10 Hz, 20 Hz and 50 Hz. The 50-Hz line-frequency peak is reduced in the preprocessed data in comparison to the raw data.



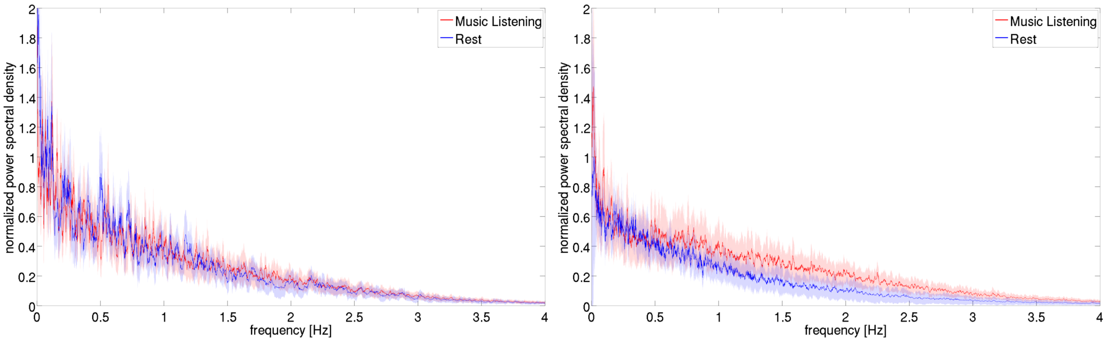

(a) raw MEG data



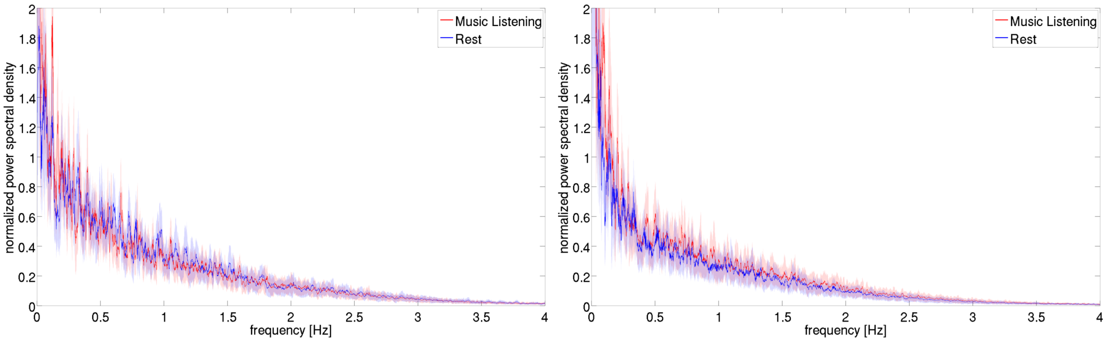

(b) preprocessed MEG data

Figure 9: Power spectral density of (a) raw and (b) preprocessed MEG data for 0–60 Hz. Shown is the mean of the music listening (red) and rest (blue) conditions surrounded by shaded areas in corresponding colors showing the standard deviations of the spectra. The two randomly chosen musicians listened to the piece by Piazzolla.

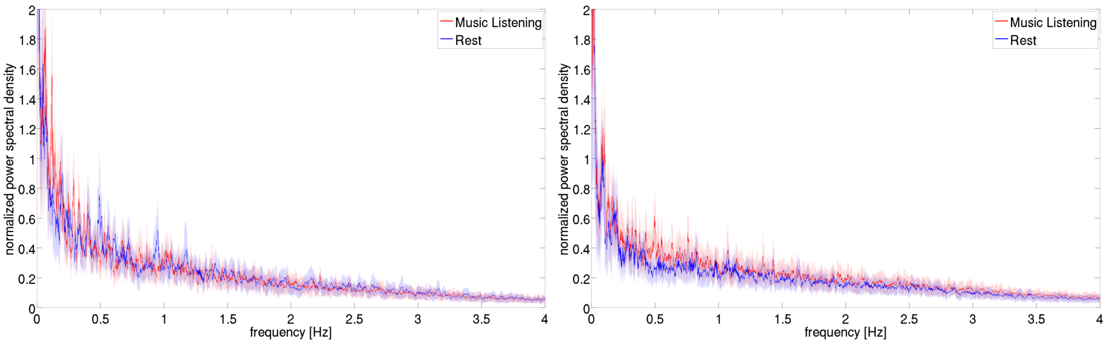
The spectra of the source-space-projected envelopes are visualized for selected frequency ranges in Figure 10. Due to the downsampling of power envelopes to 10 Hz, the spectral density is only visualized for low frequencies up to 4 Hz. Slow fluctuations dominate throughout frequency bands. The typical $1/f$ behavior is visible for both subjects. For one of the chosen subjects (left column of Figure 10), the power spectra show similar trends in both conditions. For the second chosen subject (right column of Figure 10), the music-listening condition shows higher power compared to rest in all frequency bands. In particular, the $\theta$ band (Figure 10a) and the high $\gamma$ band (Figure 10e) exhibit differences.



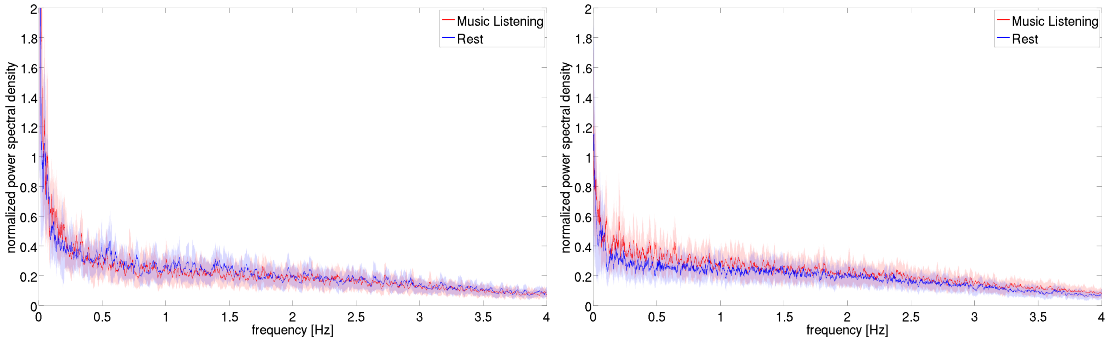

(a) $\theta$ band



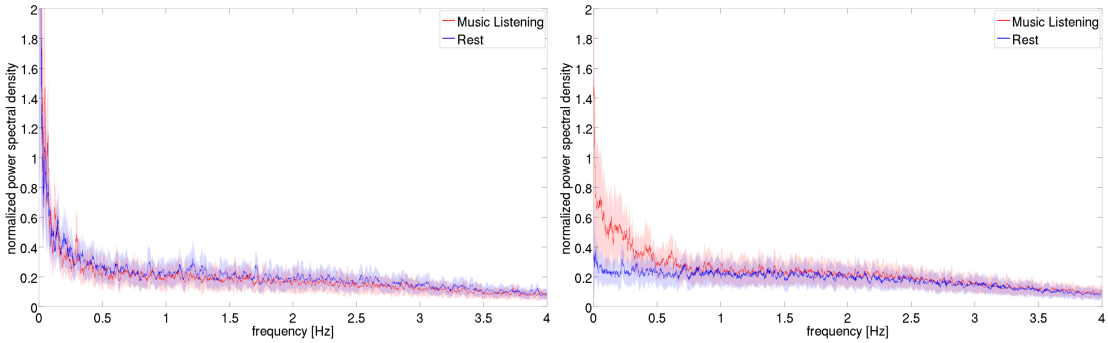

(b) $\alpha$ band




(c) $\beta$ band




(d) low $\gamma$ band




(e) high $\gamma$ band

Figure 10: Normalized power spectral density of source-space-projected power envelopes in selected frequency bands. Shown is the mean of the music listening (red) and rest (blue) conditions. The shaded areas indicate the standard deviations of the spectra. The two randomly chosen musicians (same as in Figure 9) listened to the piece by Piazzolla.

## 3.2 Envelope Time Series

An example of the envelope of a band-limited signal is shown in Figure 11. It demonstrates the method of extracting band-limited power.

Other examples of envelope time series is shown in Figures 12 and 13. The envelope time series is visualized as $z$-scores. For the computation of the $z$-score, the baseline condition was determined from empty-room MEG recordings. For visualization purposes, a zero-phase-shift filter from 0.1–1 Hz was applied. In Figure 13, the filtered envelope time series are shown for all frequency bands. An anticorrelation in the time series between $\theta$, $\alpha$ and low and high $\gamma$ bands is clearly recognizable for the two peaks in the signal (around 394 s and 423 s).

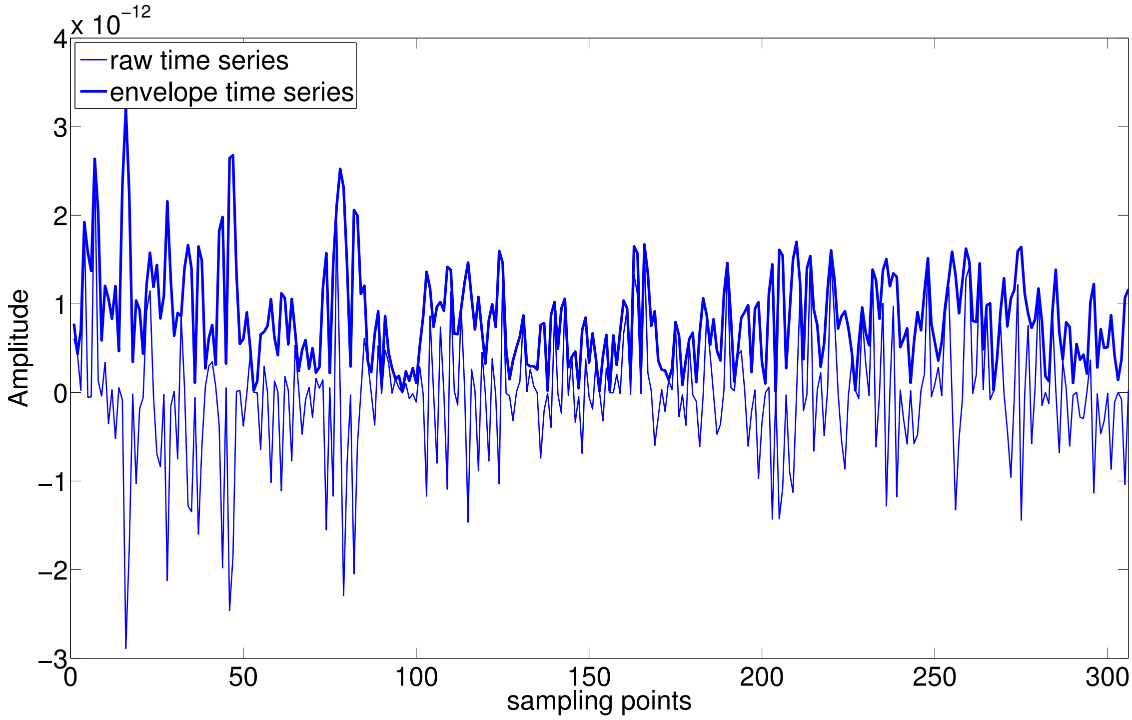



Figure 11: Envelope time series. Sensor-space time series for $\alpha$ band in one subject and one song at a randomly chosen source point. The raw time series and the absolute value of the hilbert transform (envelope) are shown.

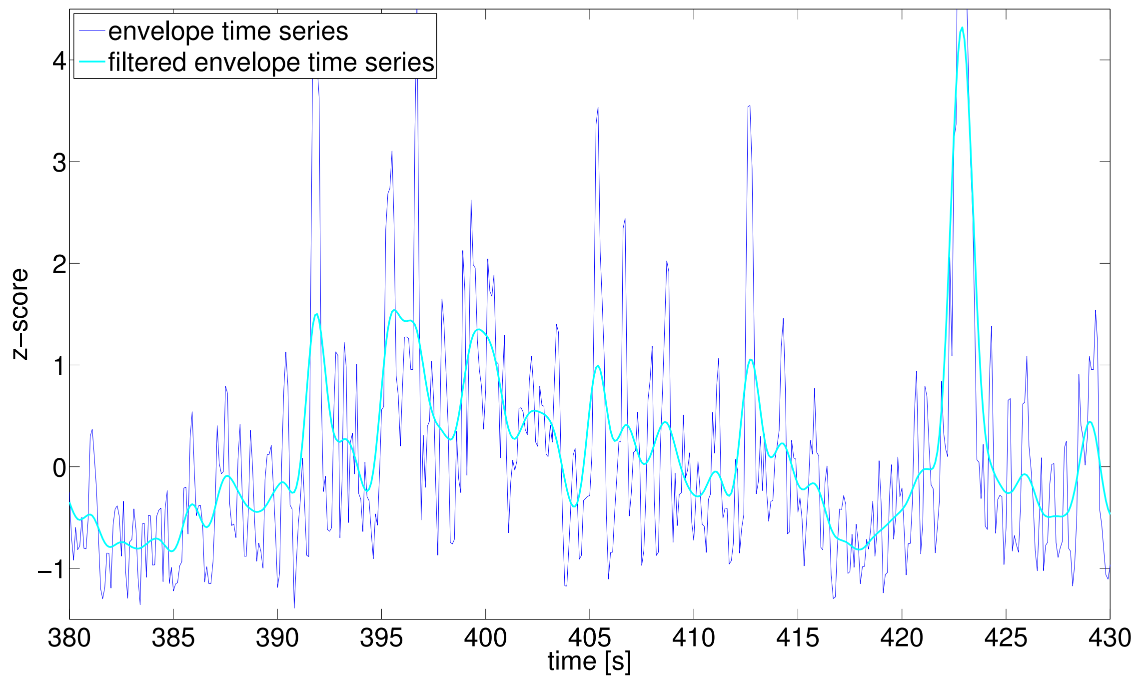



Figure 12: Envelope time series for a selected part of the Piazzolla's music piece (thin blue) compared to the time series after band-pass filtering to 0.1–1 Hz (bold turquoise). The baseline for computing the $z$-scores was the empty-room MEG recording.

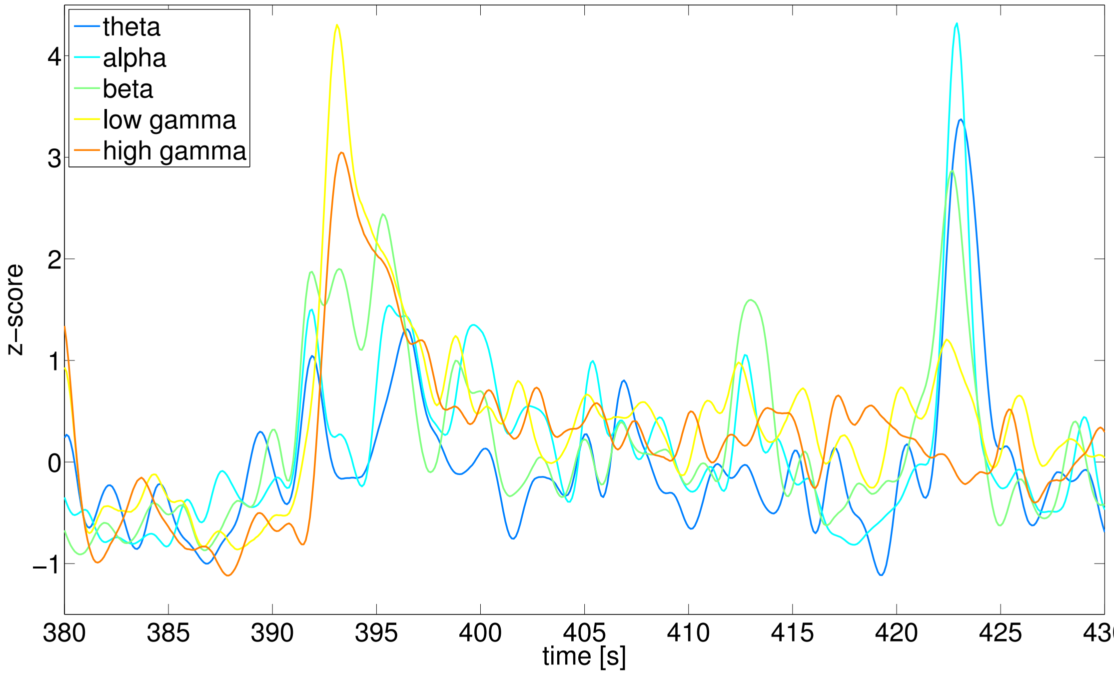



Figure 13: Filtered envelope time series for the same part of Piazzollas's music piece (as in Figure 12) for selected frequency bands. The baseline for computing the $z$-scores was the empty-room MEG recording.

## 3.3 ISC Across all Subjects

The ISC maps of group averages of all statistically significant ($p < 0.05$) pairwise correlations (9030 per music piece) computed in 20-s windows are shown in Figures 14 to 16 for selected frequency bands (Table 3).

Table 3: The frequency bands in this study.

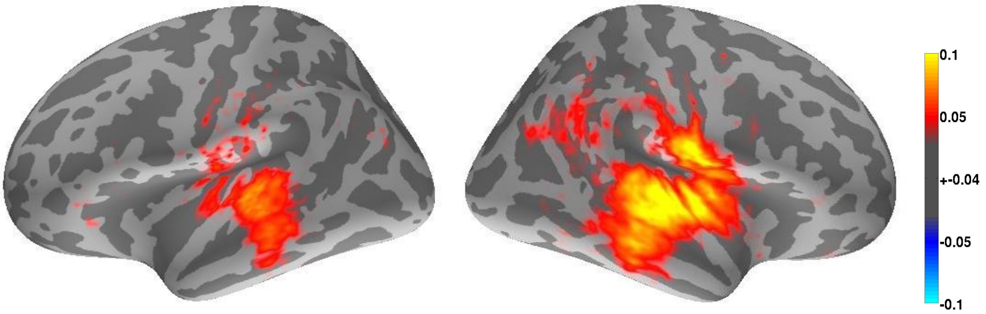
| *Band* | *Name* | *Frequency Range* |
|---|---|---|
| $\theta$ | theta | 4–8 Hz |
| $\alpha$ | alpha | 8–12 Hz |
| $\beta$ | beta | 12–25 Hz |

The ISC across all subjects are sorted by the frequency band in which they have been calculated. For each frequency band, correlation maps are shown for both hemispheres comparing the three musical stimuli and resting state. The color scales were set to show the synchronized areas and to make comparisons easier. Anatomical regions mentioned in the text have been provided by the cortical parcellation of FreeSurfer and are based on the work of Desikan et al. (2006).

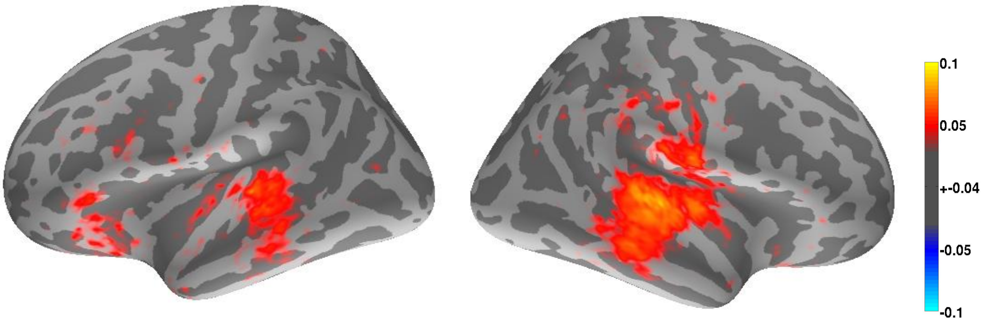
In the $\theta$ band (Figure 14), correlations up to 0.1 are found in the right transverse temporal cortex and middle and superior temporal gyri. Furthermore, right inferior pre- and postcentral gyri and right insula are synchronized by the music stimuli. In Figure 14b, the left lateral orbitofrontal cortex, pars orbitalis and pars triangularis are synchronized whereas in the other two songs these correlations are very weak. For all three musical pieces, the synchronization is strongest in the temporal areas, increased in the right compared to left hemisphere. Correlations are strongest for Piazzolla, followed by Dreamtheater and Stravinsky. The resting state shows a relatively scattered weak synchronization map, mostly in different brain regions compared to music listening conditions. The left inferior temporal gyrus shows synchronization that might lead to minor reductions in the music listening condition in this area in direct comparison.

The $\alpha$ band (Figure 15) shows highest correlation during listening to Piazzolla, too. For the two other stimuli, the correlation values stay below 0.05 and therefore, only very weak synchronization is visible in Figures 15b and 15c. The Piazzolla piece synchronizes the middle and superior temporal gyri over all subjects bilaterally, stronger in the right hemisphere. Right subcentral gyrus and insula and left pars triangularis and inferior pre- and postcentral gyri show synchronous activation. During rest, weaker and more scattered synchronizations are found, especially for left and right frontal areas, right temporal, postcentral and supramarginal gyri. In net effect, these synchronizations during rest reduce the level of synchronization, notable most during Piazzolla. Left frontal activations (pars triangularis), right frontal activations and parts of right temporal synchronizations are reduced.

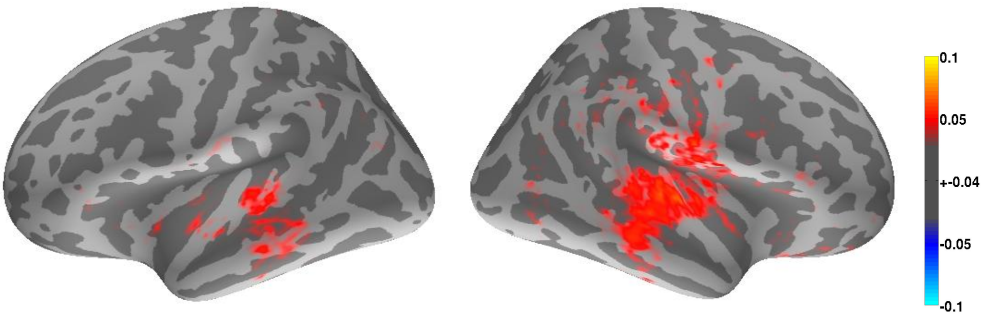
For $\beta$-band frequencies, the correlation maps (Figure 16) of all three songs show a more scattered activation without a clearly defined area. The left hemispheric



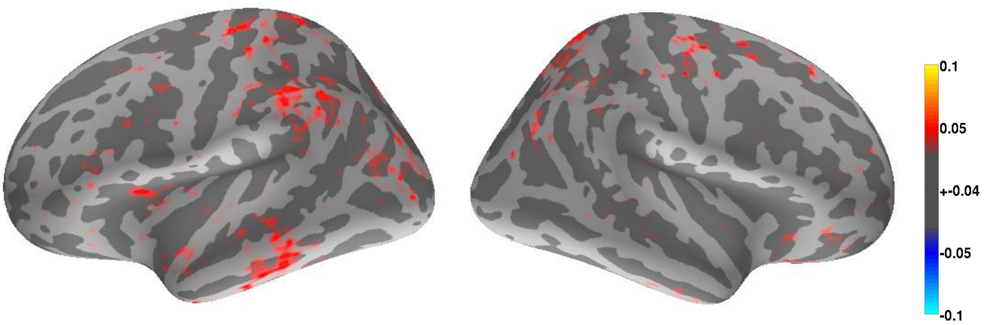

(a) Piazzolla




(b) Dreamtheater

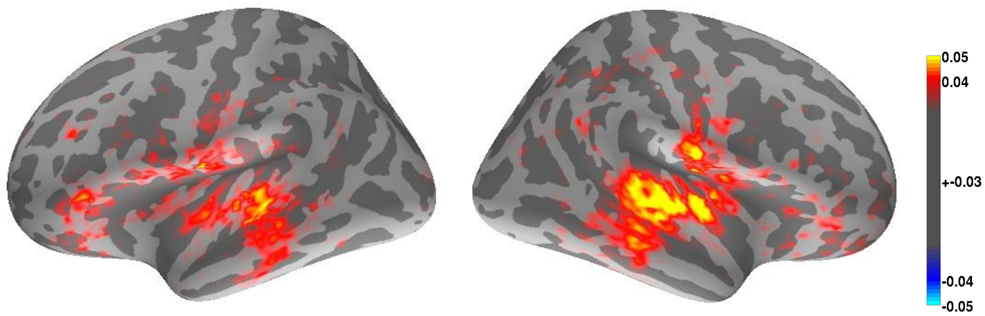



(c) Stravinsky

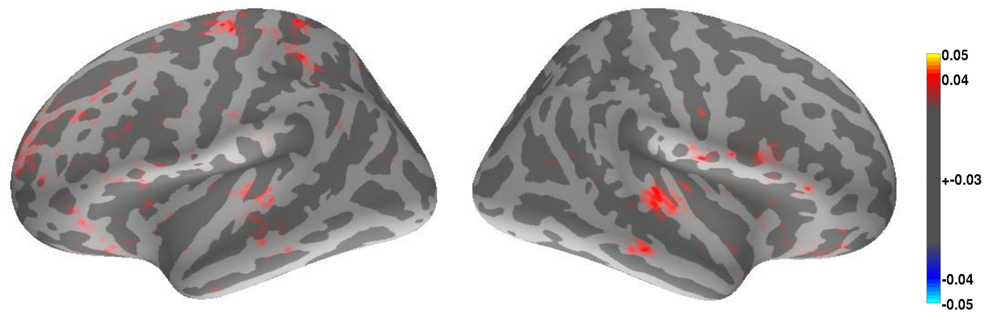



(d) Rest

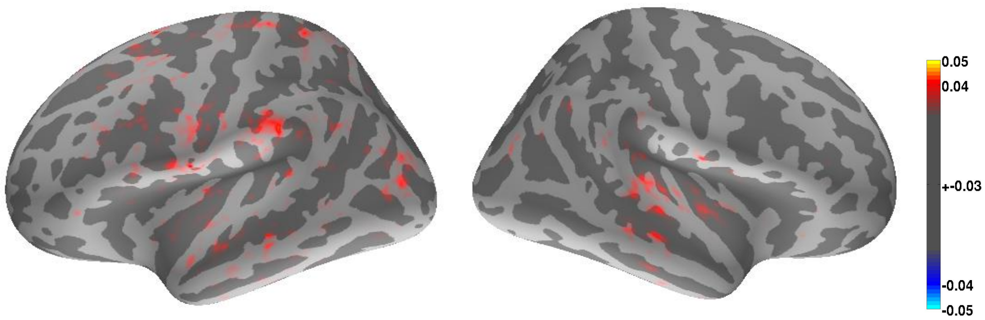
Figure 14: $\theta$ band (4–8 Hz) average inter-subject correlation maps for the three music pieces (a) Piazzolla, b) Dreamtheater, c) Stravinsky) and rest (d), eyes open) overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).



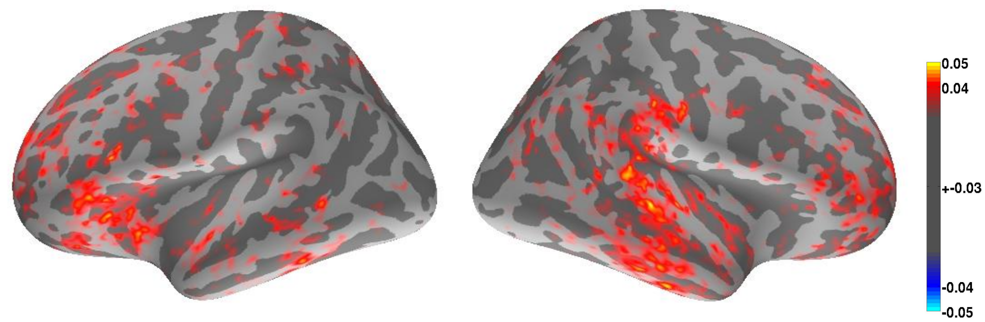

(a) Piazzolla




(b) Dreamtheater

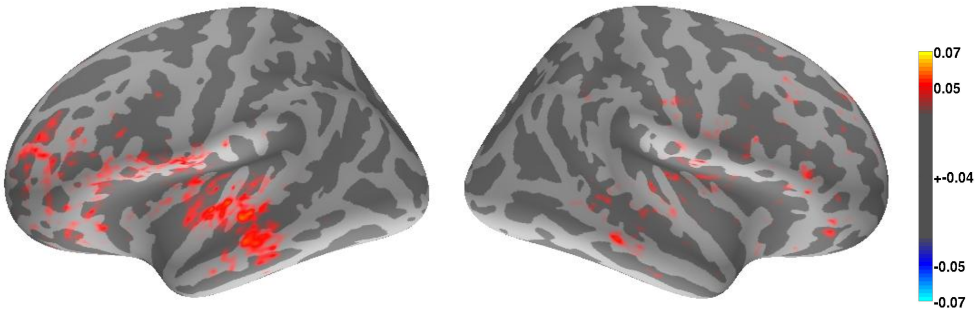



(c) Stravinsky

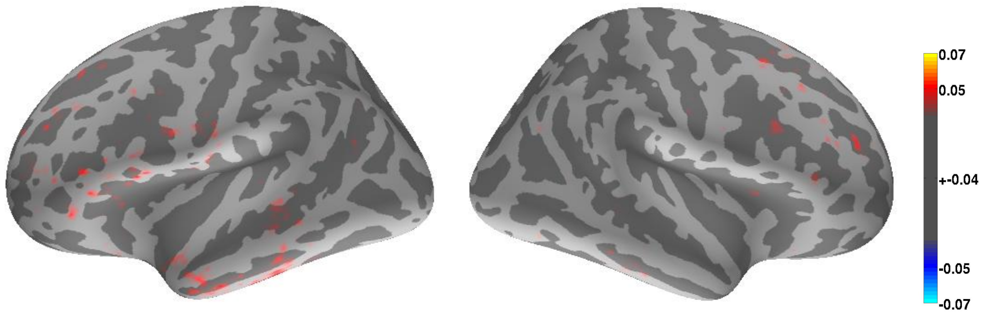



(d) Rest

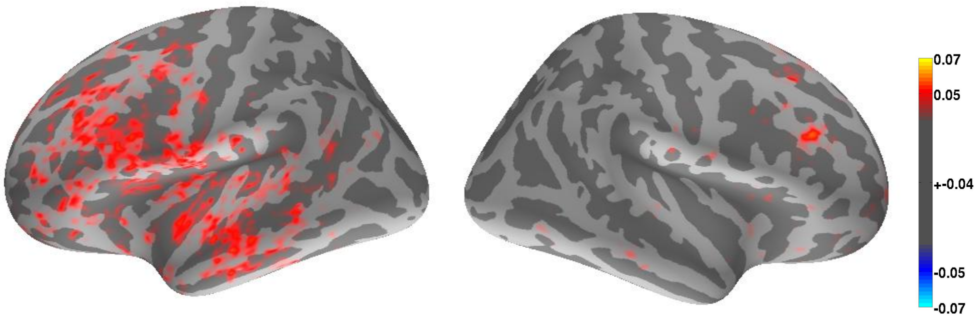
Figure 15: $\alpha$ band (8–12 Hz) average inter-subject correlation maps for the three music pieces (a) Piazzolla, b) Dreamtheater, c) Stravinsky) and rest (d), eyes open) overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).



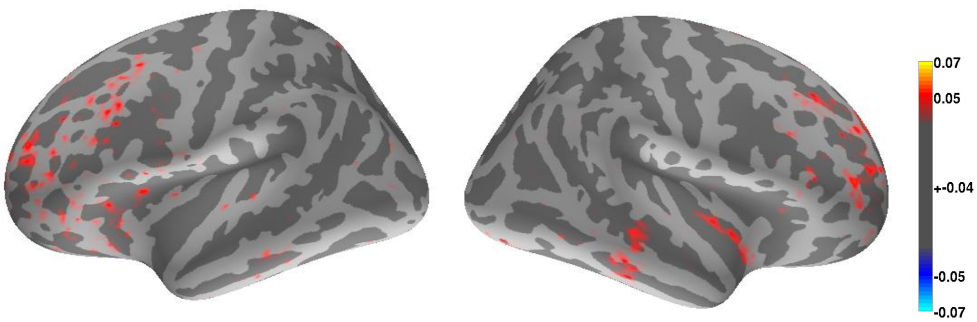

(a) Piazzolla




(b) Dreamtheater




(c) Stravinsky




(d) Rest

Figure 16: $\beta$ band (12–25 Hz) average inter-subject correlation maps for the three music pieces (a) Piazzolla, b) Dreamtheater, c) Stravinsky) and rest (d), eyes open) overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).

synchronizations are strongest during Piazzolla and Stravinsky. The right hemispheres show only weak correlations; during Piazzolla the middle temporal gyrus and during Stravinsky a small region within the rostral middle frontal gyrus are synchronized. The ISC map for listening to Dreamtheater reveals synchrony in the left inferior temporal gyrus. The active areas in the left hemisphere throughout subjects during listening to Piazzolla include the middle and superior temporal gyri, pars opercularis, pars orbitalis, pars triangularis and inferior pre- and postcentral gyri. Additionally, during listening to Stravinsky, more frontal left areas, like caudal middle frontal, rostral middle frontal and superior frontal gyri, and transverse temporal cortex show high correlation. In resting state, only few areas synchronize in the $\beta$ frequency band. Minor left and right frontal synchronizations might reduce the net synchronization during music listening, which can influence the synchronizations of left frontal areas during Piazzolla and Stravinsky (pars opercularis, pars orbitalis, pars triangularis, caudal middle frontal, rostral middle frontal gyri).

## 3.4 Comparison of ISC in Musicians and Non-musicians

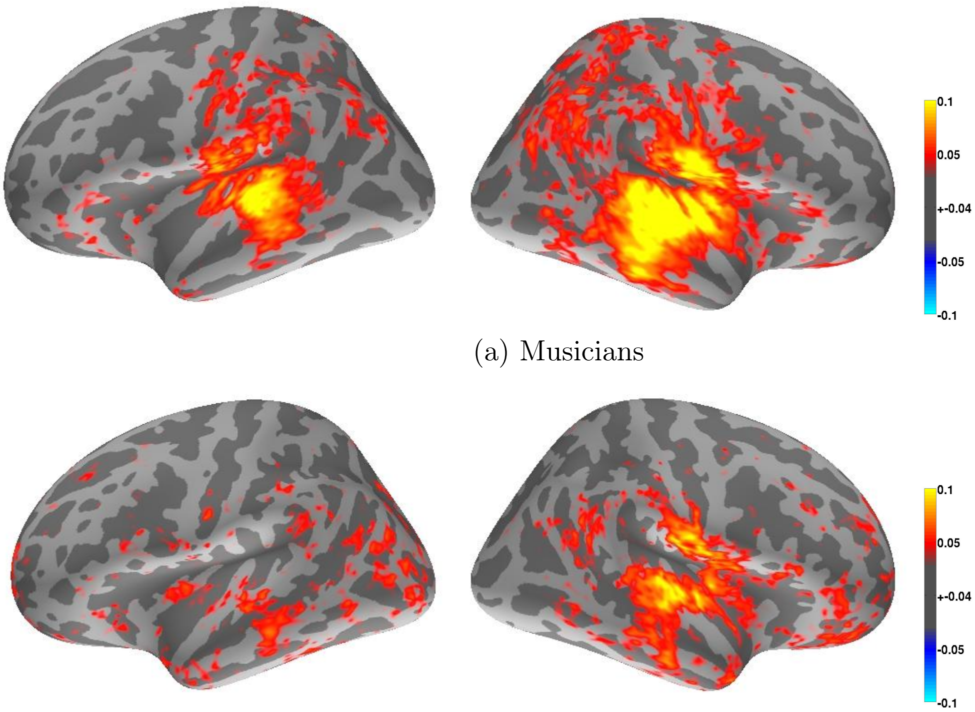
The subjects of this study were grouped by their musical expertise into musicians and non-musicians. In this section, the ISC group averages are shown for both groups for different music stimuli in the same frequency bands as introduced earlier. The goal is to compare different levels of synchronizations in cortical areas throughout the brain.

For the lowest frequency band, during listening to Piazzolla's tango (Figure 17), musicians show a stronger level of synchronization in the middle and superior temporal gyri, transverse temporal cortex and in the right banks STS. Furthermore, inferior pre- and postcentral gyri, insula and supramarginal gyrus are stronger activated across musicians' brains than in non-musicians. Right hemispheric inferior and superior parietal cortex activations are found across musicians, but not in non-musicians. Across non-musicians, slightly stronger synchrony compared to musicians is shown in the left lateral occipital and right lateral orbitofrontal cortices. However, a different ISC map is shown for Dreamtheater's song (Figure 18). Here, the synchrony in musicians concentrates in the middle and superior temporal gyri with additional activation of left pars triangularis and right inferior postcentral gyrus and insula. The brain activation of non-musicians shows synchrony of several areas spread throughout the cortex, including temporal (inferior, middle, superior gyri, transverse cortex), frontal (lateral orbital, medial orbital cortices) and parietal (superior cortex, pre- and postcentral gyri) regions. A similar ISC map to the one seen for Dreamtheater is illustrated for Stravinksy in Figure A1 (in the Appendix A). The musicians exhibit inter-subject correlations in temporal areas, slightly more widespread than during Dreamtheater, and for non-musicians, the left hemisphere shows nearly the same synchronization in temporal areas as in musicians whereas the right hemispheric synchronizations are not defined to one area. After all, for Stravinsky's music piece no very clear differences between groups can be determined.

However, to summarize the findings for the $\theta$ band for all three music pieces, the activations between musicians and non-musicians differ in a sense that the synchronization is located mainly in temporal areas for musicians and more widely spread, although also including temporal areas, for non-musicians, except during listening to Piazzolla, where synchronizations are located in similar brain areas, but they are weaker.

The Piazzolla music manifests a similar synchronization pattern in the $\alpha$ band (Figure 19) as for the $\theta$ band. Left and right temporal areas show higher synchronization for musicians with increased correlation values in the right middle and superior temporal gyri, transverse temporal cortex and posterior STS. In addition, pars triangularis, pars opercularis, left pars orbitalis, pre- and postcentral gyri, right insula and supramarginal gyri show higher synchronization across musicians. However, non-musicians exhibit higher synchronization values in lateral and medial orbitofrontal cortices and right pars orbitalis. To conclude, for Piazzolla the synchronization is stronger in mainly temporal areas in comparison to non-musicians.

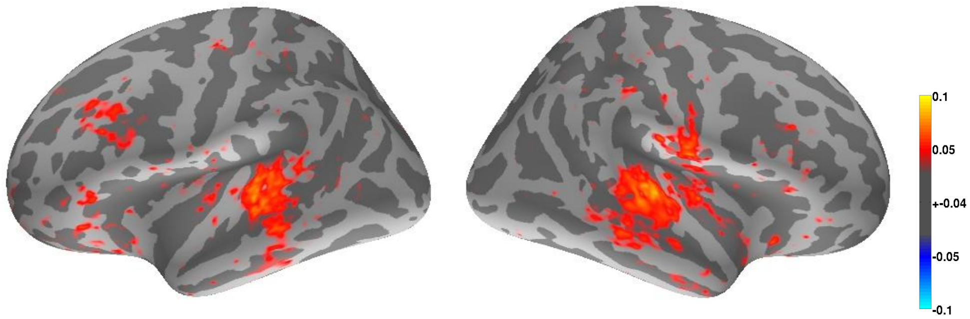
As seen before, the ISC maps depend on the song. For the Dreamtheater song (Figure 20), the musicians do not exhibit strong focal synchronizations. Only the left pre- and postcentral gyri and left superior parietal cortex seem to synchronize during listening to this progressive rock piece for musicians. Another pattern of



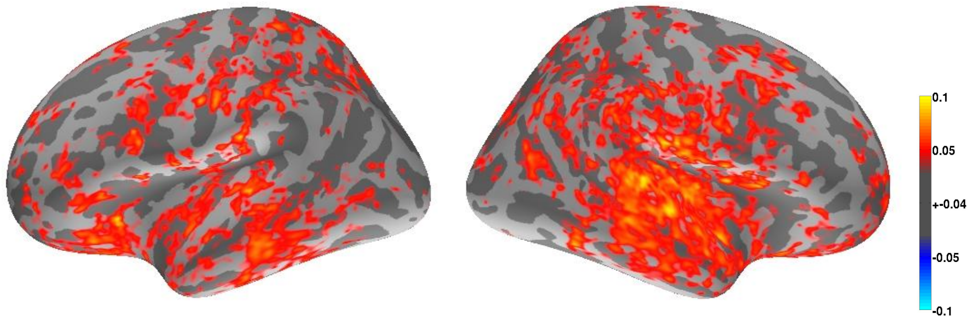

(a) Musicians

(b) Non-musicians

Figure 17: $\theta$ band (4–8 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Piazzolla overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).




(a) Musicians

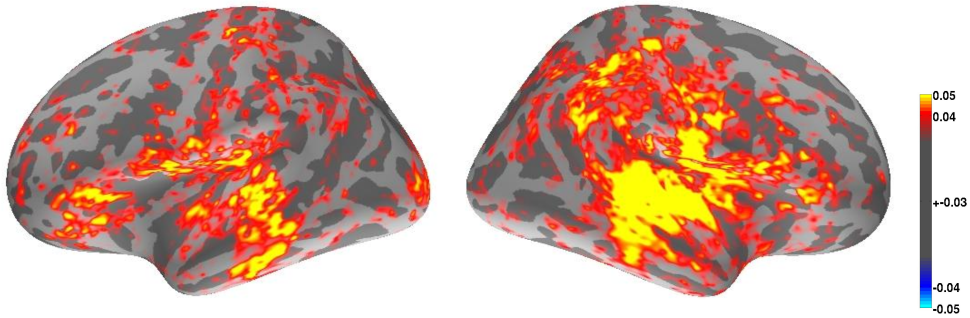



(b) Non-musicians

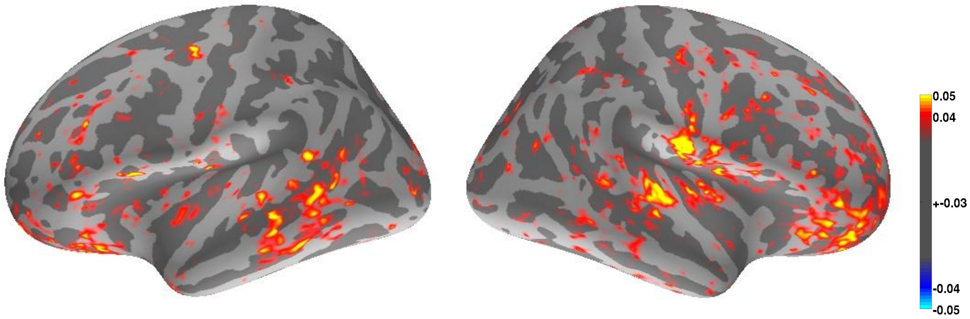
Figure 18: $\theta$ band (4–8 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Dreamtheater overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).

synchronization can be seen for non-musicians (Figure 20b), where mostly areas in the frontal regions of the brain get synchronized. Bilaterally, the lateral and medial orbitofrontal cortex, superior frontal gyri, pars opercularis, pars triangularis, middle temporal and inferior pre- and postcentral gyri exhibit stronger correlations. The right hemispheric synchronizations in non-musicians are strong in additional temporal areas (transverse cortex, STG, bank STS). A similar pattern was already found in the lower $\theta$ band for the same music piece; the non-musicians' brains synchronized stronger in especially frontal areas compared to low synchronizations overall in musicians' brains. In the last song, ISC maps (Figure A2) are very undefined and rather scattered with no focal area of synchronization. The correlation strengths show similar values, too, so that no significant differences could be detected. For this frequency band, the group comparisons between songs are very different. No common pattern during music listening can be detected. On the contrary, rather controversial results are found, if one only wants to compare the group differences during music listening in general.

In the $\beta$ band, similarity to previous activation patterns for Dreamtheater's song can be found for both Piazzolla (Figure 21) and Dreamtheater (Figure A3). Low synchronizations are revealed in musicians' brains for both, Piazzolla and Dreamtheater stimuli, although during Piazzolla a scattered weak activation can be recognized in left temporal and partly bilateral frontal areas. In non-musicians listening to Piaz-




(a) Musicians

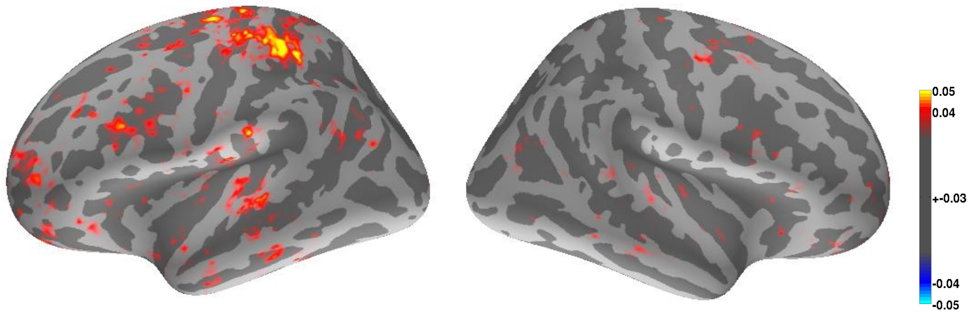



(b) Non-musicians

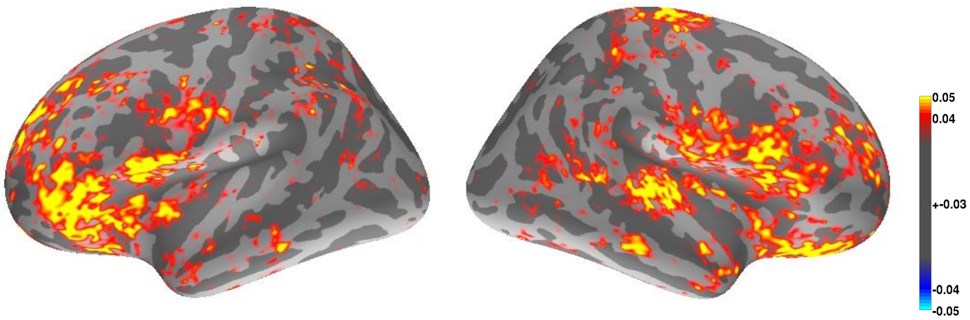
Figure 19: $\alpha$ band (8–12 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Piazzolla overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).

zolla, temporal (inferior, middle and superior gyri) and frontal areas (e.g., lateral orbitofrontal cortex), left inferior postcentral gyrus and the insula exhibit synchronization. Listening to Dreamtheater, the non-musicians show scattered activations spread in the cortex of the right hemisphere and a similar synchronization pattern as non-musicians in the right hemisphere while listening to Piazzolla, including insula, temporal and mainly frontal areas. For listening to Piazzolla and Dreamtheater, non-musicians seem to exhibit a stronger synchronization throughout the brain than musicians. The ISC maps for the Stravinsky stimulus (Figure A4) differ from the maps for the other two songs. A similar activation pattern as for the other two songs for non-musicians (Figures 21b and A3b) could be detected in this case for both musicians and non-musicians (Figures A4a and A4b, respectively). The activation pattern seems to be similar for both groups for listening to Stravinsky. Overall, for this frequency band, no common synchronization for music listening in general has been found. For Piazzolla and Dreamtheater, the synchronizations for non-musicians are stronger in several brain areas than for musicians. During listening to Stravinsky, no significant differences between groups were detected.

The resting state activity for the three frequency bands ($\theta, \alpha, \beta$) showed relatively weak synchronizations across subjects.

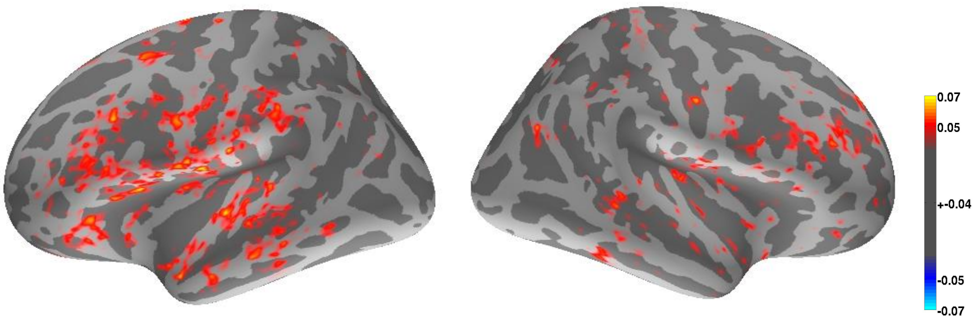



(a) Musicians

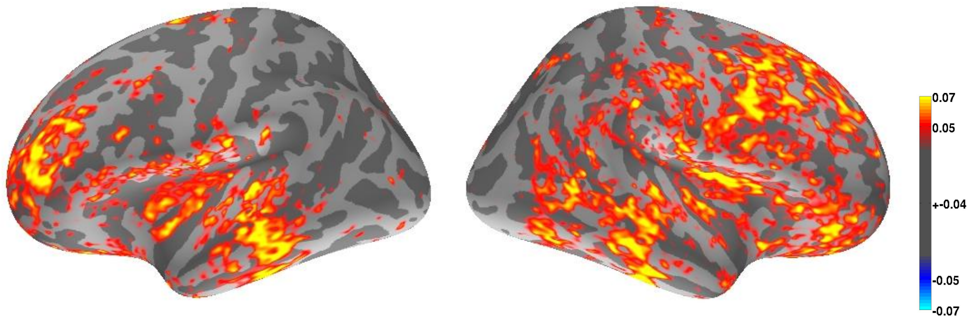



(b) Non-musicians

Figure 20: $\alpha$ band (8–12 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Dreamtheater overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).




(a) Musicians




(b) Non-musicians

Figure 21: $\beta$ band (12–25 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Piazzolla overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).

# 4 Discussion

For this study, MEG was recorded during listening to three real music pieces. It was investigated, whether listeners' brains synchronize by computing the linear, pairwise correlations of extracted power envelopes. The influence of different types of music and of musical expertise was examined.

## 4.1 ISC Across all Subjects

The power spectra of the raw MEG recordings showed expected peaks around 10 Hz, 20 Hz and 50 Hz. The 10-Hz oscillations was the expected occipital $\alpha$ activity and the 20-Hz rhythm was mainly located in somatomotor areas (Hari and Salmelin, 1997). The 50-Hz component is residual line-frequency interference. This component was reduced after the removal of eye-blink and cardiac artifacts by SSP. However, some frequency content remains even after preprocessing, which implies that the removal of high frequency artifacts can still be improved. After downsampling of the envelopes to 10 Hz, most of the frequency content remains in low frequencies.

For continuous music listening, three songs belonging to different genres have been chosen as stimuli. The elicited ISC was analyzed in different frequency bands; $\theta$ (4–8 Hz), $\alpha$ (8–12 Hz) and $\beta$ (12–25 Hz).

In the 4–8 Hz range, the temporal areas (transverse cortex, middle and superior gyri), right inferior pre- and postcentral gyri and right insula synchronized for all music pieces, stronger in the right than left hemisphere, and strongest for the Piazzolla piece. Similar results were obtained for the $\alpha$-frequency band, where only the Piazzolla piece elicited strong ISCs. For the $\beta$-frequency band, clear synchronized areas could not be defined. Left hemispheric activation during listening to Piazzolla and Stravinsky include mainly temporal areas and frontal areas, in which higher synchronization was found for Stravinsky's piece.

Continuous music listening generates strong ISC in transverse temporal cortex, middle and superior temporal gyri and insula in the $\theta$- and $\alpha$- (only during listening to Piazzolla's tango) frequency bands. Temporal areas, including superior temporal gyrus and sulcus, HG, planum temporale and polare, and insula have been found to activate synchronously during natural music listening in previous studies (Abrams et al., 2013; Alluri et al., 2012). Also other music studies that did not employ inter-subject correlation, have shown activation in similar areas (Gaab and Schlaug, 2003; Koelsch et al., 2005; Jäncke et al., 2012). Especially temporal areas were expected to be activated, as they play a role in music processing; e.g., music syntactic analysis (Koelsch, 2011), melodic representations (Platel et al., 1997; Schmithorst and Holland, 2003; Patterson et al., 2002) and analysis of timbre (Menon, 2002). The insula has been shown to respond to music stimuli (Koelsch et al., 2005; Altenmüller et al., 2014) and connected to emotional processing, e.g., during listening to pleasant versus unpleasant music (Koelsch et al., 2006) and during listening to neutral music

(Mitterschiffthaler et al., 2007). The insula is involved in autonomic regulation and integration of emotionally relevant sensory stimuli, also in music-evoked emotions (Koelsch, 2014). As the insula is a structure that is located deeper in the brain, the detection by MEG is not certain.

Therefore, for the lower frequency bands, our hypothesis can be confirmed for temporal areas and possibly for the insula. The ISCs are stronger across subjects for the right than left hemisphere. This asymmetry has been suggested earlier (Konovalov and Otmakhova, 1983; McKee et al., 1973). In several (also more recent) studies, the right hemispheric specialization for tonal processing was connected to a variety of tasks, including melodic sound processing (Patterson et al., 2002; Zatorre et al., 1994), perception and working memory for pitch (Andrade and Bhattacharya, 2003), tonal processing (Binder et al., 1997) and automatic phonetic processing of musical information (Tervaniemi et al., 2000). These processes are involved in continuous music listening and can therefore explain the right lateralized synchronizations. The left hemisphere has been suggested to be mainly responsible for rhythmic and temporal components (Bella and Peretz, 1999; Andrade and Bhattacharya, 2003). However, the question of lateralization during music processing in the brain is not completely answered yet, as musical stimuli are complex. Zatorre et al. (2002) suggested a higher temporal resolution in the left hemisphere and a better spectral resolution in the right hemisphere. However, reported lateralizations seem to vary between the studies investigating different musical features or using different experimental procedures and imaging techniques.

Synchronizations found in the $\beta$ band were weaker and not consistent throughout the music stimuli. During listening to two songs (Piazzolla and Stravinsky), left lateralized synchronizations included middle and superior temporal gyri, transverse temporal cortex, frontal areas (pars opercularis, pars orbitalis, pars triangularis, superior frontal gyrus) and inferior pre- and postcentral gyri. The found regions confirm temporal and partly inferior frontal gyrus (including pars opercularis, pars orbitalis and pars triangularis) synchronizations, as found in Abrams et al. (2013). In more detail, the superior frontal cortex is involved in pitch judgement (Schmithorst and Holland, 2003; Platel et al., 1997). Moreover, the gyri of the inferior frontal gyrus, pars triangularis, pars opercularis and pars orbitalis, have been shown to exhibit consistent activation in music studies. The pars triangularis is involved in pitch processing (Nan and Friederici, 2013) and was found to be a hub in a connectivity study related to music listening (Jäncke et al., 2012). The same study confirmed the pars opercularis as a second hub, while activation has been also found during processing of happy music without lyrics (Brattico et al., 2011). The pars orbitalis is a structure that is known to be involved in linguistic structural processing, but Levitin and Menon (2003) reasoned that it is also involved in non-linguistic processing of fine-structured stimuli. Furthermore, experiencing musical tension (Lehne et al., 2013) and rhythm complexity (Jungblut et al., 2012) involve the pars orbitalis. The pre- and postcentral gyri can relate to premotor processing. Surprisingly, only the inferior parts have shown a high synchronization, which can also be interpreted as non-motor related processing. The medial area of BA6 (Brodmann area 6, premotor area, overlapping with the found synchronizations) has been related to updating and representing verbal non-speech information (Tanaka et al., 2005). The inferior pre- and postcentral gyri have been also active during singing (Ozdemir et al., 2006). Another possibility is that the synchronizations shown for the inferior pre- and postcentral gyri result from spatial leakage of the estimated sources in the auditory cortex. As a strong source is located close to the auditory cortex, it is possible that the synchronization leaks to the spatially close inferior pre- and postcentral gyri. The visualization on the inflated brain surface implies that those regions are not located closely to each other, but anatomically they are very close. Another area that was found to be active during listening to Dreamtheater only, the left inferior temporal cortex, can also be connected to music processing, i.e., for rhythmic information processing (Bengtsson and Ullén, 2006).

The different frequency bands do show differences in music processing during continuous listening. Analyzing ISC in selected frequency bands connected to music listening is a new approach and previous electrophysiological studies can only give hints in interpreting our findings. The most clear ISCs have been found for the $\alpha$ and $\theta$ band. Both have been connected to cognitive and memory performance (e.g., Klimesch, 1999) in general as well as memory recall for music (also $\gamma$ networks, Thaut et al., 2005). The $\theta$ band has been also found to modulate activity in oscillatory networks connected to language and speech, but possibly additionally for the syntactic processing of music (Carrus et al., 2011). For the $\alpha$ band, synchronization levels throughout the brain were found to be enhanced during music listening (Wu et al., 2013). However, the majority of these studies analyzed brain networks and therefore connected music listening or music as a stimulus only to general changes of oscillation or synchronization patterns. Source modeling has not been done in most of them, and if, none of the synchronized areas found in this study has been involved. Consequently, the findings of this study provide novel techniques and insights into neuroscientific music research. The synchronized brain regions have been confirmed with previous fMRI results using the same method. To gain better understanding about the differences in frequency bands and the domains of higher-level music processing they reflect, further investigation is required.

The results of this study have been concentrated so far on the lower frequency bands, up to 25 Hz. In other music related EEG/MEG studies, the $\gamma$ band has been suggested to relate to higher-level cognitive processing in general and to music processing in specific (Sections 1.2.1 and 1.2.4). In case of successful removal of the high frequency noise without removal of neuronal signal, the $\gamma$ band is highly promising to contain valuable information about ISC during continuous music listening.

## 4.2 Influence of Music Genre

The usage of three music stimuli from different genres made it possible to identify whether listening to continuous music stimuli involved the same areas of the brain or if they differed depending on the song. As summarized earlier, the tango nuevo from

Piazzolla elicited strongest correlations across subjects for the $\theta$- and $\alpha$-frequency bands. Synchronizations for the progressive rock song from Dreamtheater and the classical ballet from Stravinsky were lower in the $\theta$ band, but evoked responses in the same areas; and very weak, so that no meaningful ISC map could be created, for the $\alpha$ band. Surprisingly, for the $\beta$ band, the ISC map for the classical music showed more synchronization in the left hemisphere than any other condition. The different activation patterns can be attributed to different levels of complexity of the stimuli, genres and the variety of musical components and features.

The tango 'Adios nonino' is most likely perceived as a complex, interesting and demanding piece to listen to and consists of several surprising events. The musical features, e.g., timbral, tonal and rhythmic features that have been extracted by Alluri et al. (2012) show a wide variation throughout the song. Less information about the musical features are available for the other two stimuli. The progressive rock song 'Stream of Consciousness' (released 2003 on the album 'Train of Thought') from Dreamtheater is a simpler music piece compared to Piazzolla's tango. Compared to other songs of the same genre, it contains more rhythmically demanding elements and might be harder to predict. In terms of musical structure, sequences and tonal variety, the song is still likely easier to comprehend than the other two songs used in this study. The piece from Stravinsky, 'Rite of Spring', is not a typical classical piece. On the contrary, in this ballet Stravinsky included novel features, such as experimental use of tonality, rhythm and dissonance variation for his time (1913). The music was described as containing a 'provocative harmonic character' and 'wildly oscillating timbres', abandoning classical melodic and harmonic development in favor of the rhythmic and timbral properties of the music, exploring the full potential of orchestral color, preventing any regular flowing rhythm, 'exaggerated' (May, 2012). With these characteristics, 'Rite of Spring' is not a predictable, typical harmonic and structured classical piece. With the musical information about the different songs the inter-subject correlations found during listening to them can be explained. As the Piazzolla piece contains the richest spectrum of musical variety, it evokes the highest level of synchronization in especially temporal areas that have been formerly connected to auditory feature processing. The consistent, reliable activations in the brain whilst listening to the modern tango are the reason why this song is one of the favorite stimuli used in cognitive music research. Listening to the two other songs does not result in strong inter-subject correlations, which can be explained by the less complex and possibly more demanding characteristics for the listeners. However, depending on the frequency band, correlations have been found in auditory cortices comparable to Piazzolla, and in left frontal areas for Stravinsky which might reflect a particular feature of the music that is represented stronger in Stravinsky than Piazzolla.

## 4.3 Influence of Musical Expertise

Different levels of synchronization during music listening are found for musicians and non-musicians. The synchronizations do not show a consistent trend, but rather vary depending on the music stimulus and frequency band as discussed above. Significant expertise-related differences are found in all frequency bands during listening to Piazzolla. In low frequency bands ($\theta$ and $\alpha$), musicians exhibit stronger synchronization in temporal areas (middle and superior temporal gyrus, transverse temporal cortex, right STS), supramarginal gyrus and right parietal areas; in which ISCs are stronger in the right hemisphere. Overall, the results confirm the hypothesis that areas found for music processing show a higher synchronization in musicians compared to non-musicians as previously suggested by Seung et al. (2005) and Jäncke et al. (2012). The right hemispheric enhancement was discussed above. The middle temporal gyrus has been activated bilaterally or right-lateralized in musicians during tonal tasks (Zatorre et al., 1998; Janata et al., 2002a) compared to non-musicians (Zatorre et al., 1994; Platel et al., 1997). In musicians trained over a long period of time, it may reflect increased multimodal integration of cognitive aspects in music processing (Seung et al., 2005). The planum temporale has been found as a hub for processing complex auditory stimuli (Griffiths and Warren, 2002) and processes auditory stimuli differently in musicians with absolute pitch (Elmer et al., 2012; Ohnishi et al., 2001). The planum polare controls auditory processing in the prosodic and attentional domain (Jäncke et al., 2001; Meyer et al., 2000). The STS is responsible for the integration of information from different modalities (Oechslin et al., 2010; Schulze et al., 2009; Hein and Knight, 2008). Activation of the supramarginal gyrus stronger in musicians during music listening has been also found by Seung et al. (2005). The left-lateralized activation of this areas has been found during active listening to a music piece, connected to selective attention (Janata et al., 2002b). Consequently, the higher activation in musicians may result from a more attentive listening to the music. It might also reflect a different way of processing musical input in terms of pitch. Musicians have showed positive correlations in the supramarginal gyrus for a pitch memory task whereas non-musicians have seemed to rely more on brain regions important for pitch discrimination (Gaab and Schlaug, 2003). The superior parietal cortex is involved in auditory processing, as shown by previous studies (Gaab and Schlaug, 2003; Satoh et al., 2001). A higher activation in musicians has also been connected to selective attention during auditory processing (Satoh et al., 2001). The inferior parietal cortex has been more synchronous in musicians and has been previously shown to be involved in a pitch judgement task (Schmithorst and Holland, 2003; Platel et al., 1997), where differences in pitches had to be detected in a comparison of melodies. It has been suggested that musicians employ a visual mental strategy in the interval processing.

Musicians listening to Dreamtheater synchronized their brains in the same areas as found during Piazzolla in the $\theta$ band, but did not show significant correlations for the $\alpha$ band. Non-musicians listening to the same song, however, showed a surprisingly widespread high synchronization pattern for both low frequency bands in frontal regions. For the $\beta$ band, musicians' brains only synchronized weakly in scattered left hemispheric regions during listening to Piazzolla. On the contrary, non-musicians showed high correlations that are spread bilaterally. In general, non-musicians seemed to show higher synchronizations in the $\beta$ frequency range than musicians. Comparing the synchronization maps for the third stimulus (Stravinsky) did not reveal clear differences in activations for musicians' and non-musicians' brains for any of the selected frequency bands.

Non-musicians showed a higher synchronization in the lateral orbitofrontal cortex for listening to Piazzolla and in a variety of other frontal areas as well as temporal and parietal regions for listening to Dreamtheater and Stravinsky. Activation of temporal areas can be explained by processing music stimuli and sequences in general (see above). The superior frontal cortex is relevant for attending to the musical stimuli in non-musicians, as found previously by Schmithorst and Holland (2003). The lateral orbitofrontal cortex has been found to play a role in processing of emotion in the music domain as a response to unexpected harmonic functions (Koelsch et al., 2005). Tension can build up by listening to unexpected chords that only relate distantly to the current key, which activates orbitofrontal cortex and amygdala (Lehne et al., 2013). As musicians are more experienced with unexpected key changes, these areas might not be involved in their musical processing stream. On the contrary, non-musicians might not have a broad spectrum of experience in listening to this kind of music and consequently build up tension. The involvement of parietal regions has been discussed above.

ISC maps do not show overall consistent synchronizations across all subjects or groups. The differences of the musical pieces used in this study have been explained above and they might be one factor. High synchronizations for both groups during listening to Piazzolla in comparison to the other two pieces can be explained by the complexity of the tango and the variety of musical features that make it an excellent music stimulus to elicit activity in auditory processing areas. On the contrary, for other music pieces no significant differences could be determined in group comparisons. To conclude, the inter-subject synchronizations cannot be summarized for one general 'music listening' condition (versus rest), but should rather be interpreted for each music piece differently. However, similarities have been found, too, and the interpretation has been concentrated on those similar synchronies. For many brain regions involved in continuous music listening the hypotheses have been confirmed. Areas in which no significant activations have been found are the intraparietal and inferior frontal sulci, motor areas, like mid-cingulate cortex and premotor cortex, and emotion-related regions, for example left anterior cingulate and parahippocampal gyrus. Especially the absence of motor cortical activations is surprising for musicians, as listening to music as a professional is known to involve processing dependent on the played instrument.

## 4.4 Limitations of the Chosen Methods

The choice of frequency bands relied on commonly used ranges for the known oscillatory activity in the brain. For band-pass filtering, conservative filters were used and they did not exhibit a sharp cut-off. Therefore, the neighbouring ranges can influence the selected frequency band. For example, synchronizations in $\theta$- and $\alpha$-frequency bands show similar patterns. It is possible to use a different kind of filtering method to apply sharper cut-offs or select different frequency ranges for the analysis.

MEG is known for its excellent temporal resolution, but its spatial resolution is limited. Applying the L2-minimum-norm estimation, the spatial extend of projected sources cannot be determined absolutely. The visualized estimated are blurred, and consequently, spatial leakage can occur. For example, if one of two close regions in the cortex exhibits high activation, this activation can spread to the other area. Whether the activation results from one or two focal points cannot directly be answered. Due to the visualization on the inflated brain surface, the two anatomically close areas can appear to be in distant locations, although they are not. More accurate solutions for the inverse problem are investigated, which will likely improve spatial resolution in MEG in the future.

# 5 Conclusion and Future Directions

ISC is a data-driven approach that does not require *a priori* assumptions. Here, a linear, pair-wise correlation of power envelopes was computed to detect synchronizations across subjects during music listening. For complex stimuli, ISC has been used successfully for fMRI, but only scarcely for MEG.

Continuous music listening elicited significant ISCs for low-frequency bands ($\theta$ and $\alpha$) in middle and superior temporal gyri and transverse temporal cortex stronger in the right than left hemisphere. Synchronizations in the $\beta$ band were weaker, but confirmed the involvement of temporal and fronto-parietal (precentral sulcus, inferior frontal gyrus) areas. Of the three real-world musical pieces, the modern tango from Piazzolla elicited strongest correlations across subjects. It is considered an excellent music stimulus to elicit activity in music processing areas in the brain, because of its complexity and variety of musical features. The synchronized areas were concordant with fMRI findings related to music listening, but using MEG they provide novel insight into neuroscientific music research.

A group comparison dependent on the level of musical expertise (musicians versus non-musicians) confirmed differences in ISCs during listening to Piazzolla's tango especially in the low frequency bands. Musicians exhibited stronger synchronization in temporal areas (middle and superior temporal gyri, transverse temporal cortex, right STS), supramarginal gyrus and parietal cortices (right inferior and superior). Again, right hemispheric lateralization could be observed. Non-musicians showed higher ISCs in frontal areas, e.g., lateral orbitofrontal cortex as well as temporal and parietal regions. However, no common trend of synchronizations for all songs could be detected. Consequently, the group comparisons have to be looked at song-specifically.

To summarize, auditory processing areas synchronize during listening to continuous music stimuli. The extend of synchronization differs depending on the selected frequency band and music stimulus. For the song that elicited highest ISCs across all subjects, musicians showed an increased synchrony in auditory processing areas compared to non-musicians in low frequency bands.

Future work should be carried out to investigate the best possible methodology to study ISC for MEG data. The $\gamma$-band frequency should be studied as well. Further investigation is needed in the interpretation of findings throughout different frequency bands in general and for cognitive music research specifically. The improvement of spatial resolution in MEG would yield high expectations to model sources with improved certainty on the cortical brain surface.

ISC analysis has been shown to meet expectations for analyzing data from continuous music listening. It is considered a valuable tool for future brain research utilizing MEG, especially for analyzing complex stimuli. Listening to music as a complex stimulus induces brain-to-brain coupling in which both the genre of music and the musical expertise of the listener influence the area of shared brain activity.

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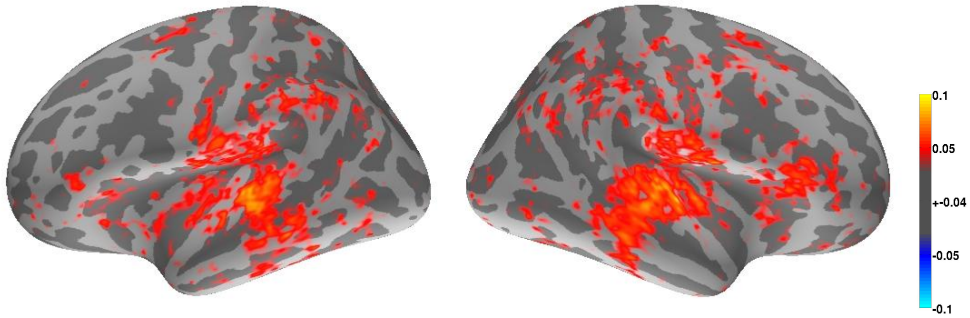
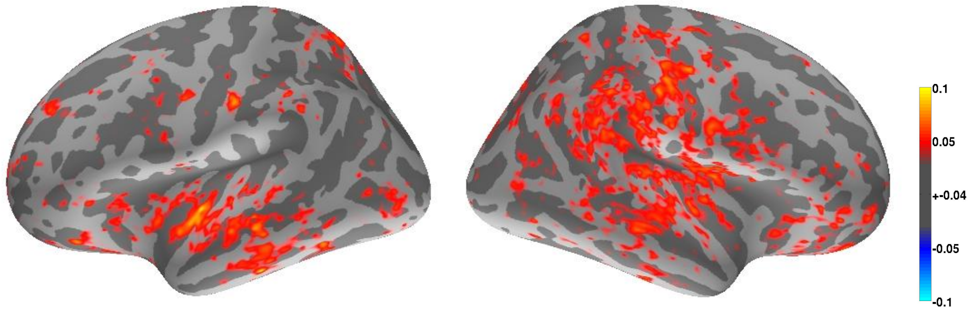
# A Additional ISC Maps Comparing Musicians and Non-musicians

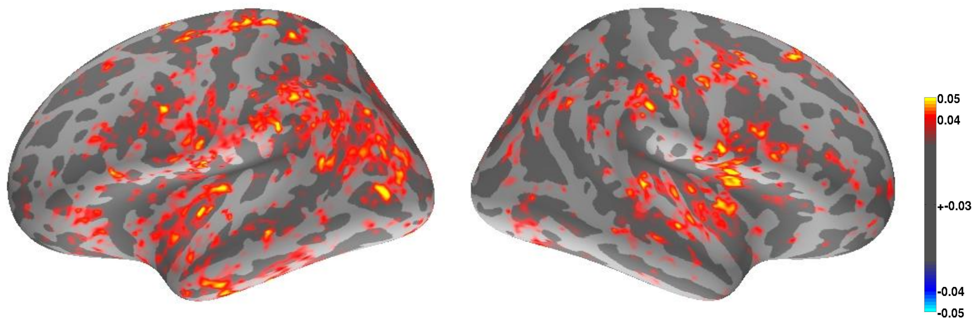



(a) Musicians

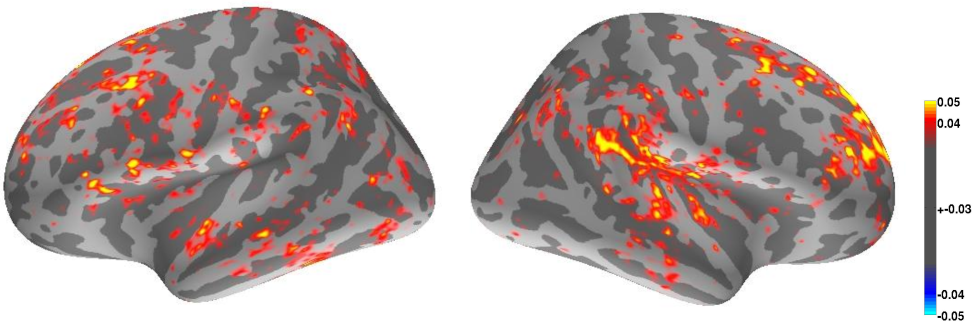



(b) Non-musicians

Figure A1: $\theta$ band (4–8 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Stravinsky overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).

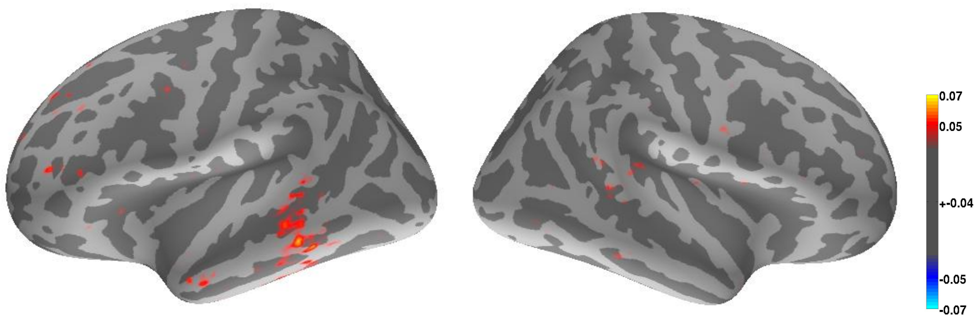



(a) Musicians

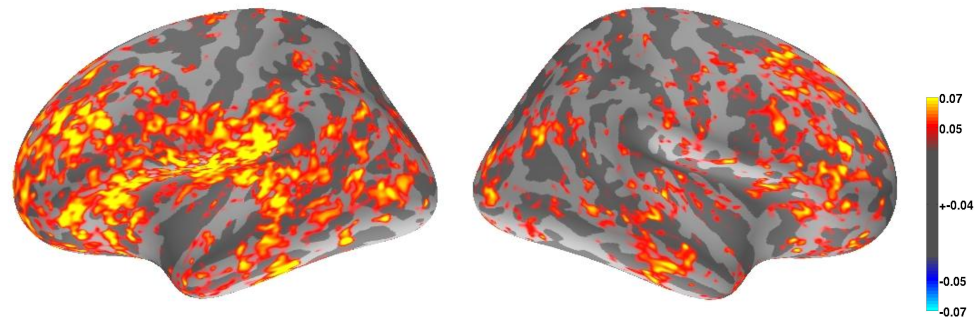



(b) Non-musicians

Figure A2: $\alpha$ band (8–12 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Stravinsky overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).

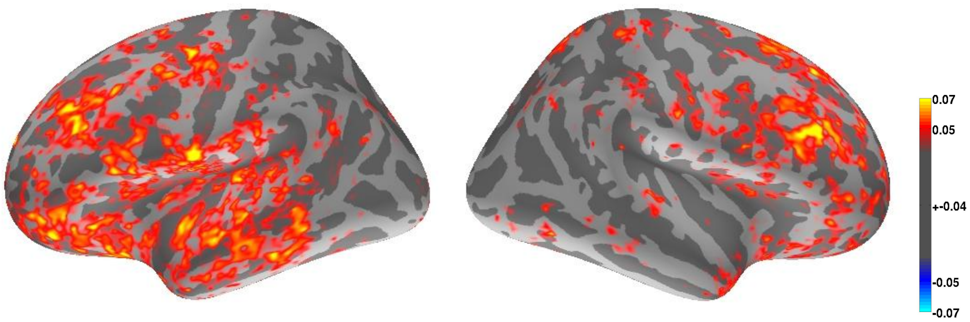



(a) Musicians

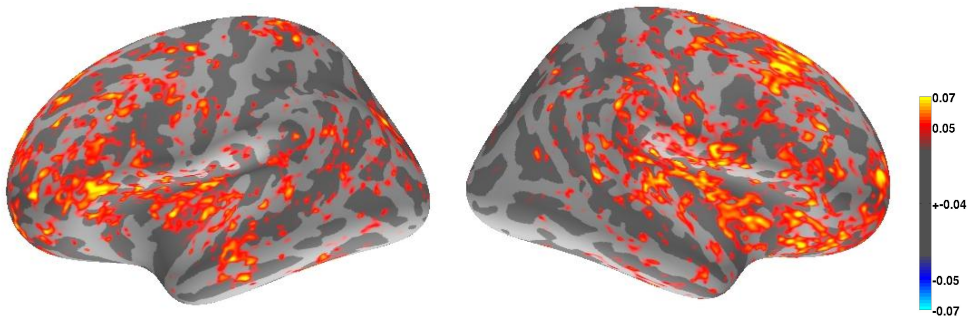



(b) Non-musicians

Figure A3: $\beta$ band (12–25 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Dreamtheater overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).




(a) Musicians




(b) Non-musicians

Figure A4: $\beta$ band (12–25 Hz) average inter-subject correlation maps comparing musicians (a) and non-musicians (b) during listening to Stravinsky overlaid on FreeSurfer's *fsaverage* brain (left: left hemisphere, right: right hemisphere).